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(54) Title: TREATMENT OF NEUROPATHIC PAIN WITH 6H-PYRROLO[3,4-D]PYRIDAZINE COMPOUNDS

(57) Abstract: 6*H*-pyrrolo[3,4-d]pyridazine compounds and methods of their use of as ligands of voltage gated calcium channels (VGCC), useful in the treatment of neuropathic pain, and psychiatric and mood disorders such as, for example, schizophrenia, anxiety, depression, panic, and bipolar disorder, as well as in the treatment of pain, Parkinson s disease, cognitive dysfunction, epilepsy, circadian rhythm disorders, drug addiction, drug abuse, drug withdrawal and other

TITLE OF THE INVENTION

TREATMENT OF NEUROPATHIC PAIN WITH 6H-PYRROLO[3,4-D]PYRIDAZINE COMPOUNDS

BACKGROUND OF THE INVENTION

FIELD OF THE INVENTION

The present invention is directed 6*H*-pyrrolo[3,4-*d*]pyridazine compounds and method of their use. In particular, this invention is directed to a method of use of 6*H*-pyrrolo[3,4-*d*]pyridazine compounds in the treatment of neuropathic pain.

RELATED BACKGROUND

A major mechanism in many physiological processes, including neurotransmission in the mammalian nervous system, is the opening and closing of voltage gated calcium channels ("VGCC"), also known as voltage sensitive calcium channels ("VSCC") . Such VGCC are formed by the asssembly of subunit classes such as alpha 1 and alpha 2. One subunit in the alpha 2 class is the $\alpha 2\delta$ subunit. The activity of the calcium channel can be modulated by the activities of the component subunits. For example, gabapentin is known to bind with high affinity to the $\alpha 2\delta$ subunit. Four isoforms of this $\alpha_2\delta$ protein are known and gabapentin binds with high affinity to 2 of these ($\alpha_2\delta$-1 and $\alpha_2\delta$-2). The relative importance of these two activities in accounting for the efficacy and adverse effects of gabapentin is not known. Compounds that display high-affinity binding to the $\alpha 2\delta$ subunit of voltage gated calcium channels have been shown to be efficacious for the treatment of, for example, neuropathic pain. See, *J. Biol. Chem.*, 271(10):5768-5776(1996) and *J. Med. Chem.*, 41:1838-1845(1998). Nonetheless, if one isoform is more controlling of the channel modulation, while the other is less, then compounds that are selective to the controlling isoform are likely to be more efficacious and display fewer side-effects.

Thus, it is desirable to identify other compounds that display high-affinity binding to the $\alpha 2\delta$ subunit of voltage gated calcium channels to provide new medicines in the treatment of neuropathic pain. Further, such compounds can be useful in the treatment of psychiatric and mood disorders such as, for example,

schizophrenia, anxiety, depression, bipolar disorders, and panic, as well as in the treatment of pain, Parkinson's disease, cognitive dysfunction, epilepsy, circadian rhythm and sleep disorders – such as shift-work induced sleep disorder and jet-lag, drug addiction, drug abuse, drug withdrawal and other diseases.

International Patent Publication No. WO 01/88101describes a cell line for the expression of an $\alpha_2\delta 2$ calcium channel subunit.

6-Methyl-6*H*-pyrrolo[3,4-*d*]pyridazine is described in MM.J. Duflos et al., *Tetrahedron Lett.*, 3453-3454(1973). 1,4,5,7-tetramethyl-6-phenyl-6*H*-pyrrolo[3,4-*d*]pyridazine, 1,4,5-trimethyl-6,7-diphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine, 5,7-dimethyl-1,4,6-triphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine, 5-methyl-1,4,6,7-tetraphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine, 1,4-bis-(4-methoxy-phenyl)-5,7-dimethyl-6-phenyl-6*H*-pyrrolo[3,4-*d*]pyridazine, 1,4-bis-(4-methoxy-phenyl)-5-methyl-6,7-diphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine, and 1,4-diethyl-5,7-dimethyl-6-phenyl-6*H*-pyrrolo[3,4-*d*]pyridazine are described in R. Rips et al., *J. Org. Chem.*, 24:551-554(1959). 1,4,5,7-Tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine, *N*-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-benzamide, 1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-ylamine picrate, and 1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-ylamine are described in W.L. Mosby, *J. Chem. Soc.*, 3997-4003(1957). 5,7-Dimethyl-6-phenyl-6*H*-pyrrolo[3,4-*d*]pyridazine is described in R.Rips et al., *J. Org. Chem.*, 24:372-374(1959).

5,7-Dimethyl-2-phenacyl-6*H*-pyrrolo[3,4-*d*]pyridazinium bromide (also known as 5,7-dimethyl-2-(2-oxo-2-phenyl-ethyl)-6*H*-pyrrolo[3,4-*d*]pyridazin-2-ium bromide) and 2-(2-methoxycarbonylvinyl)-5,7-dimethyl-6*H*-pyrrolo[3,4-*d*]pyridazinium tetrafloroborate are described in F. Fuentes-Rodriguez et al., *J. Chem. Res. Miniprint*, 11:2901-2914(1987). 5,7-Diphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine is described in T. Hernandez et al., *J. Chem. Soc., Perkins Trans.*, 1:899-902(1985), and F.F. Rodriguez et al., *J.Chem. Res. Miniprint*, 11:3001-3001(1987). 5,6,7-Trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine is described in T. Hernandez et al., *J. Chem. Soc., Perkin Trans.*, 1:899-902(1985), F. Fuentes-Rodriguez et al., *J. Chem. Res. Miniprint*, 11:2901-2914(1987), and R. von Kreher et al., *Agnew Chem.*, 82:958(1970).

1,4-Diphenyl-7,8,9,10-tetrahydro-pyridazino[4,5-*a*]indolizine (also known as 1,4-diphenyl-5,6,7,8-tetrahydro-2,3,8a-triaza-fluorene) and 5-methyl-1,4-diphenyl-7,8,9,10-tetrahydro-pyridazino[4,5-*a*]indolizine (also known as 9-methyl-1,4-diphenyl-5,6,7,8-tetrahydro-2,3,8a-triaza-fluorene) are described in T. Uchida et al., *J. Heterocycl. Chem.*, 15:1303-1307(1978). 6-Benzyl-1,4-diphenyl-5-p-tolyl-6*H*-

pyrrolo[3,4-*d*]pyridazine, 6-benzyl-5-(2-chloro-phenyl)-1,4-diphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine, 1,4,5,6,7-pentaphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine, 6,7,10,11-tetraphenyl-pyridazino[4',5':3,4]pyrrolo[1,2-*a*]quinoxaline (also known as 6,7,10,11-tetraphenyl-5,8,9,11a-tetraaza-benzo[*a*]fluorene), 11-(4-nitro-phenyl)-6,7,10-triphenyl-pyridazino[4'.5':3,4]pyrrolo[1,2-*a*]quinoxaline (also known as 11-(4-nitro-phenyl)6,7,10-triphenyl-5,8,9,11a-tetraaza-benzo[*a*]fluorene), and 6-benzyl-1,4,5-triphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine are described in T. Uchida et al., *J. Heterocycl. Chem.*, 15:241-248(1978).

9,12-Diphenyl-pyridazino[4',5':3,4]pyrrolo[2,1-*a*]isoquinoline, 5-methylsulfanyl-1,4,6,7-tetraphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine, and 1,4,6,7-tetraphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine-5-carboxylic acid ethyl ester are described in K.T. Potts et al., *J. Org. Chem.*, 42:1639-1644(1977). 7,10-Diphenyl-pyridazino[4',5':3,4]pyrrolo[1,2-*a*]quinoline, and 11,14-diphenyl-pyridazino[4',5':3,4]pyrrolo[1,2-*f*]phenanthridine (also known as 9,12-diphenyl-10,11,13a-triaza-indeno[1,2-*l*]phenanthrene) are described in K.T. Potts et al., *J. Org. Chem.*, 44:977-979(1979).

1-Oxo-7-oxy-6b,11b-dihydro(pyridazino[4',5'-c]-pyrrolo)[2.1-c]benzoxazine-1,4 (also known as 11-hydroxy-5-oxa-8,9,11a-triaza-benzo[*a*]fluoren-6-one) is described in Kumashiro et al., *Nippon Kagaku Zasshi.*, 82:1072-1074(1961).

10-Methyl-1,4-diphenyl-8,9-dihydro-7H-benzo(ef)pyridazino[4,5-a]cycl[3.3.2]azine, and 11-methyl-1,4-diphenyl-7,8,9,10-tetrahydrocyclohepta(ef)pyridazino[4,5-a]cycl[3.3.2]azine are described in M. Noguchi et al., *J.Heterocycl. Chem.*, 22:1049-1053(1985).

1,4-Dichloro-5,6,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine, 1-chloro-4-ethoxy-5,6,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine, 1-chloro-5,6,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazinium chloride, 1-ethoxy-2,5,6,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazinium tetrafluoroborate, 1-ethoxy-5,6,7-trimethyl-2*H*,6*H*-pyrrolo[3,4-*d*]pyridazinium tetrafluoroborate, 1-ethoxy-3-ethyl-5,6,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazinium tetrafluoroborate, and 1-ethoxy-5,6,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine are described in S. Inel et al., *Tetrahedron*, 40:3979-3986(1984).

5-Cyano-1,4-dimethylpyridazino[4,5-*a*]indolizine (also known as 1,4-dimethyl-2,3,8a-triaza-fluorene-9-carbonitrile), 1,4-dimethyl-6-phenyl-2,3,8a-triaza-fluorene-9-carbonitrile, 6-benzolyl-1,4-dimethyl-2,3,8a-triaza-fluorene-9-carbonitrile, 6-benzyl-1,4-diphenyl-2,3,8a-triaza-fluorene-9-carbonitrile, and 1,4,6-trimethyl-2,3,8a-triaza-fluorene-9-carbonitrile are described in K. Matsumoto et al., *J.*

Heterocycl. Chem., 25:1793-1801(1988). 5-Cyano-1,4-diphenylpyridazino[4,5-*a*]indolizine (also known as 1,4-diphenyl-2,3,8a-triaza-fluorene-9-carbonitrile) is described in K. Matsumoto et al., *J. Heterocycl. Chem.*, 25:1793-1801(1988), and K. Matsumoto et al., *Heterocycles*, 20:1525-1529(1983). 6-Methyl-1,4-diphenyl-2,3,8a-triaza-fluorene-9-carbonitrile, 6-benzoyl-1,4-diphenyl-2,3,8a-triaza-fluorene-9-carbonitrile, and 1,4,6-triphenyl-2,3,8a-triaza-fluorene-9-carbonitrile are described in K. Matsumoto et al., *J. Heterocycl. Chem.*, 25:1793-1801(1988), K. Matsumoto et al., *Heterocycles*, 34:2239-2242(1992), K. Matsumoto et al., *Heterocycles*, 20:1525-1529(1983), and K. Matsumoto et al., *Can. J. Chem.*, 71:529-533(1993). 5,7-Dimethyl-1,4-diphenyl-2,3,8a-triaza-fluorene-9-carbonitrile, and 9,12-diphenyl-pyridazino[4',5':3,4]pyrrolo[2,1-*a*]isoquinoline-8-carbonitrile are described in K. Matsumoto et al., *Heterocycles*, 34:2239-2242(1992), and K. Matsumoto et al., *Can. J. Chem.*, 71:529-533(1993).

Dimethyl 3,12,13,17-tetramethyl-7^2,7^3-diazabenzo[g]porphyrin-2,18-dipropionate is described in I.A. Chaudhry et al., *Aust. J. Chem.*, 35:1185-11201(1982). 5,6-Dihydro-2,3-dimethoxypyridazino[4',5':3,4]pyrrolo[2,1-*a*]isochinolin-9-ol, 5,6-dihydro-2,3-dimethoxypyridazino[4',5':3,4]pyrrolo[2,1-*a*]isochinolin-9-ol-hydrochloride, and 3-methyl-6,9-diphenylthiazolo[3',2':1,2]pyrrolo[3,4-*d*]pyridine (also known as 1-methyl-4,7-diphenyl-3-thia-5,6,8a-triaza-cyclopenta[*a*]indene) are described in W. Losel et al., *Chem. Ber.*, 118:413-427 (1985). 1,4-Diphenylpyridazino[4',5':3,4]pyrrolo[2,1-*b*]benzothiazole (also known as 1,4-diphenyl-5-thia-2,3,9b-triaza-indeno[2,1-*a*]indene) is described in N. Abe et al., *Bull. Chem. Soc. Japan*, 55:200-203(1982).

Nevertheless, there is a need to identify 6H-pyrrolo[3,4-d]pyridazine compounds that display high-affinity binding – particularly selective binding - to the $\alpha_2\delta$ subunit of voltage gated calcium channels to provide new medicines in the treatment of neuropathic pain, as well as psychiatric and mood disorders such as, for example, schizophrenia, anxiety, depression, bipolar disorders, and panic, as well as in the treatment of pain, Parkinson's disease, cognitive dysfunction, epilepsy, circadian rhythm and sleep disorders – such as shift-work induced sleep disorder and jet-lag, drug addiction, drug abuse, drug withdrawal and other diseases.

SUMMARY OF THE INVENTION

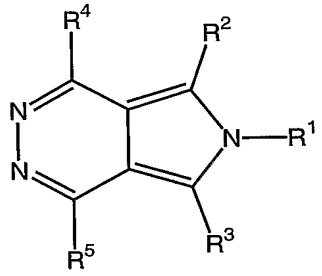
The present invention is directed to a method of use of 6*H*-pyrrolo[3,4-*d*]pyridazine compounds in the treatment of neuropathic pain. The present invention

is also directed to the use of 6*H*-pyrrolo[3,4-*d*]pyridazine compounds in the treatment of psychiatric and mood disorders such as, for example, schizophrenia, anxiety, depression, bipolar disorders, and panic, as well as in the treatment of pain, Parkinson's disease, cognitive dysfunction, epilepsy, circadian rhythm and sleep disorders – such as shift-work induced sleep disorder and jet-lag, drug addiction, drug abuse, drug withdrawal and other diseases. The present invention is also directed to novel 6*H*-pyrrolo[3,4-*d*]pyridazine compounds that selectively bind to $\alpha_2\delta$-1 subunit of Ca channels.

DETAILED DESCRIPTION OF THE INVENTION

A method of treatment of neuropathic pain, and treatment of psychiatric and mood disorders such as, for example, schizophrenia, anxiety, depression, bipolar disorders, and panic, as well as the treatment of pain, Parkinson's disease, cognitive dysfunction, epilepsy, circadian rhythm and sleep disorders – such as shift-work induced sleep disorder and jet-lag, drug addiction, drug abuse, and drug withdrawal of the present invention comprising a step of

administering an effective amount of a compound represented by Formula (I):



(I)

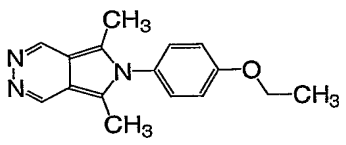
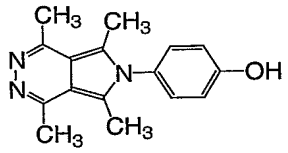
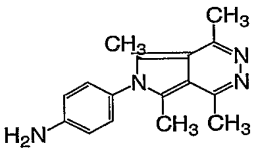
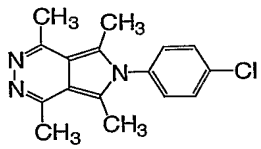
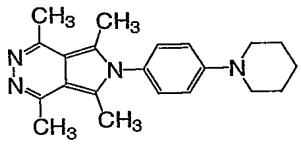
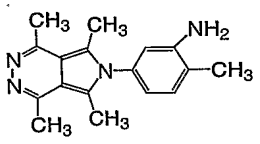
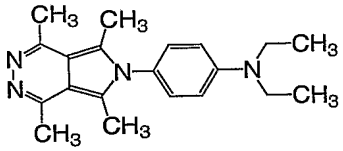
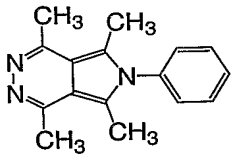
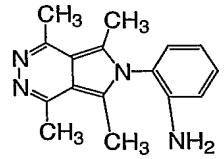
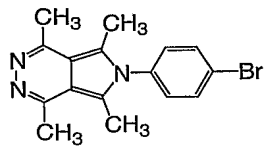
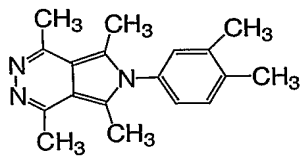
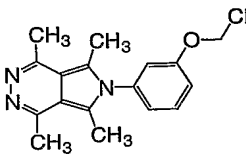
or a pharmaceutically acceptable salt thereof, wherein

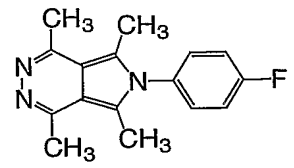
R1 is –C0-6alkyl–aryl, –C0-6alkyl–heteroaryl, –C0-6alkyl–C3-6cycloalkyl, or –C0-6alkyl–heteroC3-7cycloalkyl, optionally substituted with 1-6 independent halogen, –CN, NO_2, -C1-6alkyl, –C0-6alkyl–C3-6cycloalkyl, –C0-6alkyl–heteroC3-7cycloalkyl, $-OR^6$, $-NR^6R^7$, $-C(=NR^6)NR^7R^8$, $-N(-NR^{88}R^6)NR^7R^8$, $-NR^6COR^7$, $-NR^6CO_2R^7$, $-NR^6SO_2R^{88}$, $-NR^6CONR^7R^8$, $-SR^{88}$, $-SOR^{88}$, $-SO_2R^{88}$, $-SO_2NR^6R^7$, $-COR^6$, $-CO_2R^6$, $-CONR^6R^7$, $-C(=NR^6)R^7$, or $-C(=NOR^6)R^7$ substituents;

R^2, R^4, R^3, and R^5 each independently is $-C_{0-6}$alkyl, $-C_{0-6}$alkyl–aryl, $-C_{0-6}$alkyl–heteroaryl, $-C_{0-6}$alkyl–C_{3-6}cycloalkyl, or $-C_{0-6}$alkyl–heteroC_{3-7}cycloalkyl, optionally substituted with 1-6 independent halogen, –CN, NO_2, $-C_{1-6}$alkyl, $-OR^6$, $-NR^6R^7$, $-C(=NR^6)NR^7R^8$, $-N(-NR^{88}R^6)NR^7R^8$, $-NR^6COR^7$, $-NR^6CO_2R^7$, $-NR^6SO_2R^{88}$, $-NR^6CONR^7R^8$, $-SR^{88}$, $-SOR^{88}$, $-SO_2R^{88}$, $-SO_2NR^6R^7$, $-COR^6$, $-CO_2R^6$, $-CONR^6R^7$, $-C(=NR^6)R^7$, or $-C(=NOR^6)R^7$ substituents;

R^6, R^7, R^8, and R^{88} each independently is $-C_{0-6}$alkyl, $-C_{3-7}$cycloalkyl, heteroaryl, or aryl; optionally substituted with 1-5 independent halogen, –CN, $-C_{1-6}$alkyl, $-O(C_{0-6}$alkyl), $-O(C_{3-7}$cycloalkyl), -O(aryl), $-N(C_{0-6}$alkyl)(C_{0-6}alkyl), $-N(C_{0-6}$alkyl)(C_{3-7}cycloalkyl), or $-N(C_{0-6}$alkyl)(aryl) substituents; and

provided that the compound is not selected from the following table:

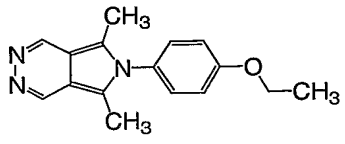
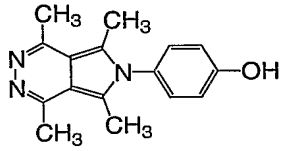
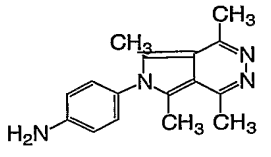
In one aspect, the method of this invention administers an effective amount of a compound represented by Formula (I), or a pharmaceutically acceptable salt thereof, wherein

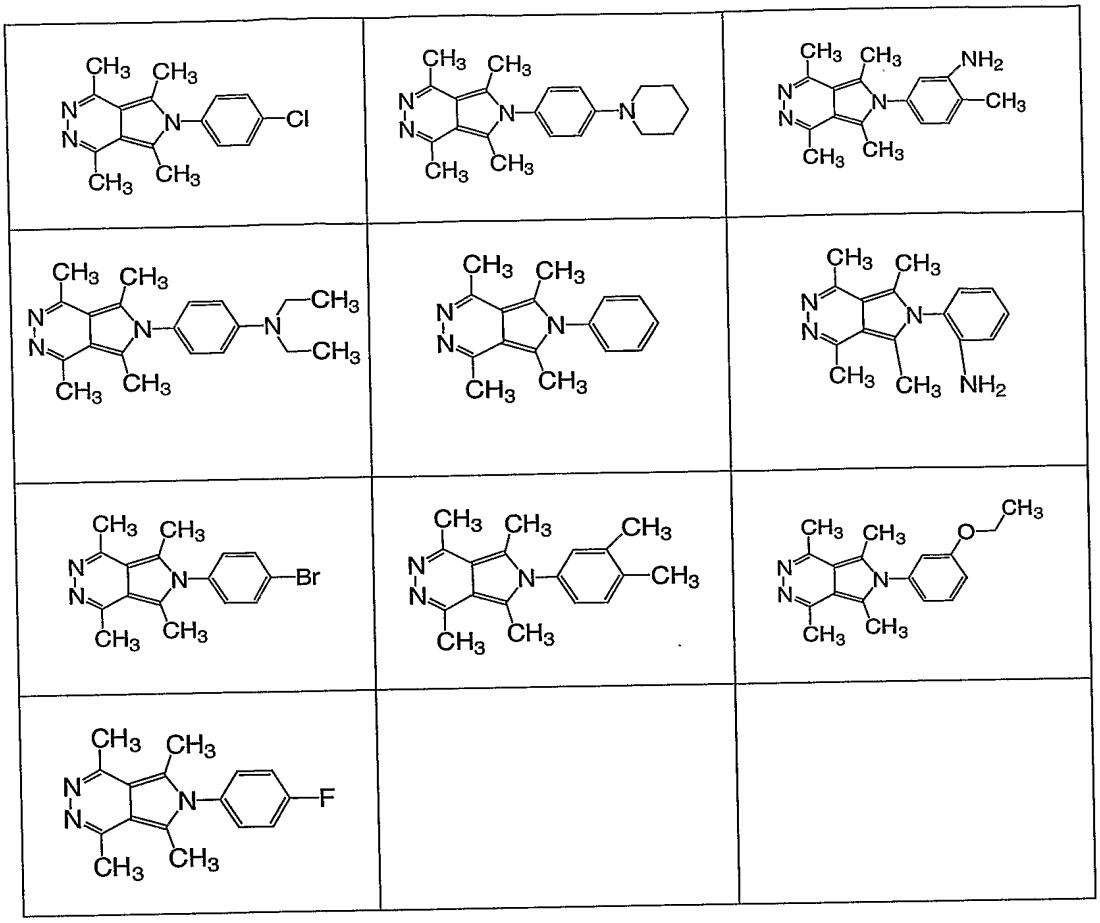
R^1 is $-C_{0-6}$alkyl–aryl optionally substituted with 1-6 independent halogen, –CN, NO_2, $-C_{1-6}$alkyl, $-C_{0-6}$alkyl–C_{3-6}cycloalkyl, $-C_{0-6}$alkyl–heteroC$_{3-7}$cycloalkyl, $-OR^6$, $-NR^6R^7$, $-C(=NR^6)NR^7R^8$, $-N(-NR^{88}R^6)NR^7R^8$, $-NR^6COR^7$, $-NR^6CO_2R^7$, $-NR^6SO_2R^{88}$, $-NR^6CONR^7R^8$, $-SR^{88}$, $-SOR^{88}$, $-SO_2R^{88}$, $-SO_2NR^6R^7$, $-COR^6$, $-CO_2R^6$, $-CONR^6R^7$, $-C(=NR^6)R^7$, or $-C(=NOR^6)R^7$ substituents;

R^2, R^4, R^3, and R^5 each independently is $-C_{0-6}$alkyl, $-C_{0-6}$alkyl–aryl, $-C_{0-6}$alkyl–heteroaryl, $-C_{0-6}$alkyl–C_{3-6}cycloalkyl, or $-C_{0-6}$alkyl–heteroC$_{3-7}$cycloalkyl, optionally substituted with 1-6 independent halogen, –CN, NO_2, $-C_{1-6}$alkyl, $-OR^6$, $-NR^6R^7$, $-C(=NR^6)NR^7R^8$, $-N(-NR^{88}R^6)NR^7R^8$, $-NR^6COR^7$, $-NR^6CO_2R^7$, $-NR^6SO_2R^{88}$, $-NR^6CONR^7R^8$, $-SR^{88}$, $-SOR^{88}$, $-SO_2R^{88}$, $-SO_2NR^6R^7$, $-COR^6$, $-CO_2R^6$, $-CONR^6R^7$, $-C(=NR^6)R^7$, or $-C(=NOR^6)R^7$ substituents;

R^6, R^7, R^8, and R^{88} each independently is $-C_{0-6}$alkyl, $-C_{3-7}$cycloalkyl, heteroaryl, or aryl; optionally substituted with 1-5 independent halogen, -CN, $-C_{1-6}$alkyl, $-O(C_{0-6}$alkyl), $-O(C_{3-7}$cycloalkyl), -O(aryl), $-N(C_{0-6}$alkyl)(C_{0-6}alkyl), $-N(C_{0-6}$alkyl)(C_{3-7}cycloalkyl), or $-N(C_{0-6}$alkyl)(aryl) substituents; and

provided that the compound is not selected from the following table:



In an embodiment of this one aspect, the method of this invention administers an effective amount of a compound represented by Formula (I), or a pharmaceutically acceptable salt thereof, wherein

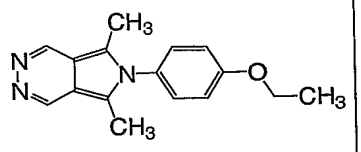
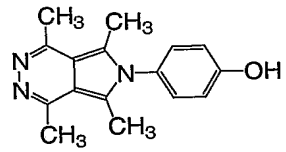
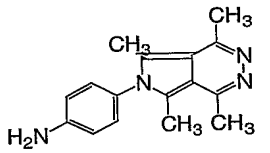
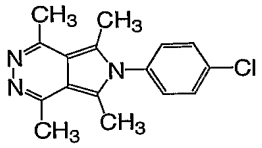
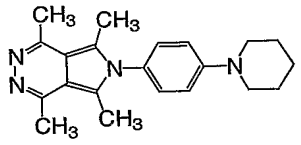
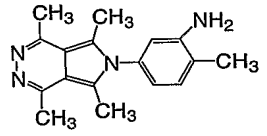
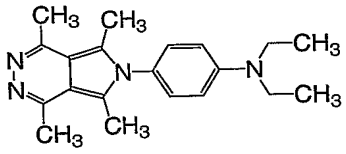
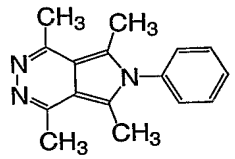
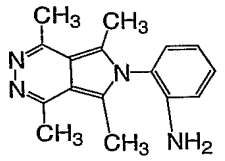
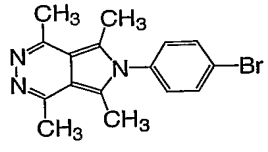
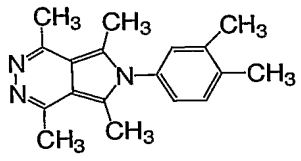
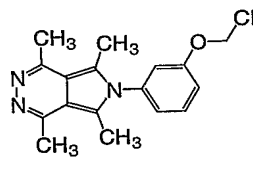
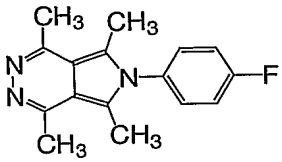
R^1 is $-C_{0-6}$alkyl–phenyl optionally substituted with 1-6 independent halogen, –CN, NO_2, $-C_{1-6}$alkyl, $-C_{0-6}$alkyl–C_{3-6}cycloalkyl, $-C_{0-6}$alkyl–heteroC_{3-7}cycloalkyl, $-OR^6$, $-NR^6R^7$, $-C(=NR^6)NR^7R^8$, $-N(-NR^{88}R^6)NR^7R^8$, $-NR^6COR^7$, $-NR^6CO_2R^7$, $-NR^6SO_2R^{88}$, $-NR^6CONR^7R^8$, $-SR^{88}$, $-SOR^{88}$, $-SO_2R^{88}$, $-SO_2NR^6R^7$, $-COR^6$, $-CO_2R^6$, $-CONR^6R^7$, $-C(=NR^6)R^7$, or $-C(=NOR^6)R^7$ substituents;

R^2, R^4, R^3, and R^5 each independently is $-C_{0-6}$alkyl, $-C_{0-6}$alkyl–aryl, $-C_{0-6}$alkyl–heteroaryl, $-C_{0-6}$alkyl–C_{3-6}cycloalkyl, or $-C_{0-6}$alkyl–heteroC_{3-7}cycloalkyl, optionally substituted with 1-6 independent halogen, –CN, NO_2, $-C_{1-6}$alkyl, $-OR^6$, $-NR^6R^7$, $-C(=NR^6)NR^7R^8$, $-N(-NR^{88}R^6)NR^7R^8$, $-NR^6COR^7$,

$-NR^6CO_2R^7$, $-NR^6SO_2R^{88}$, $-NR^6CONR^7R^8$, $-SR^{88}$, $-SOR^{88}$, $-SO_2R^{88}$, $-SO_2NR^6R^7$, $-COR^6$, $-CO_2R^6$, $-CONR^6R^7$, $-C(=NR^6)R^7$, or $-C(=NOR^6)R^7$ substituents;

R^6, R^7, R^8, and R^{88} each independently is $-C_{0-6}$alkyl, $-C_{3-7}$cycloalkyl, heteroaryl, or aryl; optionally substituted with 1-5 independent halogen, -CN, $-C_{1-6}$alkyl, $-O(C_{0-6}$alkyl), $-O(C_{3-7}$cycloalkyl), -O(aryl), $-N(C_{0-6}$alkyl)(C_{0-6}alkyl), $-N(C_{0-6}$alkyl)(C_{3-7}cycloalkyl), or $-N(C_{0-6}$alkyl)(aryl) substituents; and

provided that the compound is not selected from the following table:

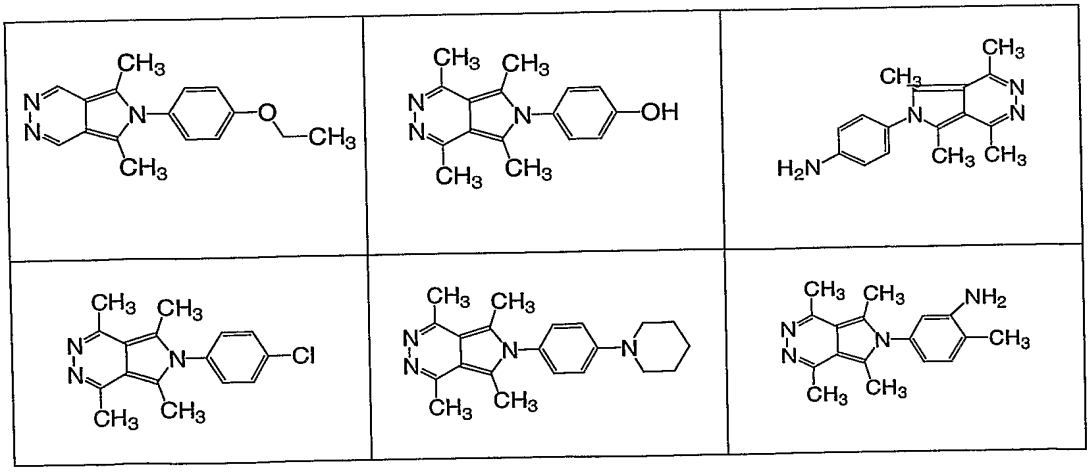
In another embodiment of this one aspect, the method of this invention administers an effective amount of a compound represented by Formula (I), or a pharmaceutically acceptable salt thereof, wherein

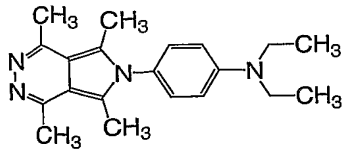
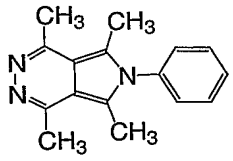
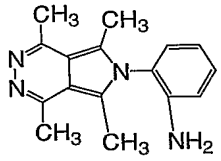
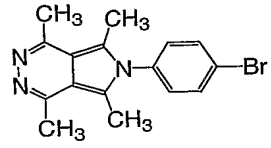
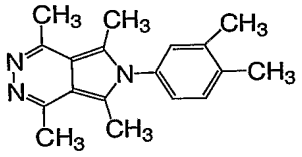
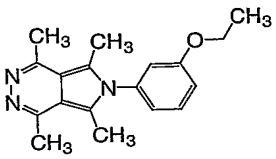
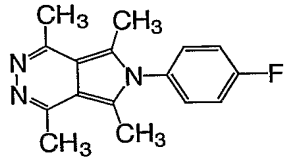
R^1 is $-C_{0-6}$alkyl–phenyl optionally substituted with 1-6 independent halogen, –CN, NO_2, $-C_{1-6}$alkyl, $-C_{0-6}$alkyl–C_{3-6}cycloalkyl, $-C_{0-6}$alkyl–heteroC_{3-7}cycloalkyl, $-OR^6$, $-NR^6R^7$, $-C(=NR^6)NR^7R^8$, $-N(-NR^{88}R^6)NR^7R^8$, $-NR^6COR^7$, $-NR^6CO_2R^7$, $-NR^6SO_2R^{88}$, $-NR^6CONR^7R^8$, $-SR^{88}$, $-SOR^{88}$, $-SO_2R^{88}$, $-SO_2NR^6R^7$, $-COR^6$, $-CO_2R^6$, $-CONR^6R^7$, $-C(=NR^6)R^7$, or $-C(=NOR^6)R^7$ substituents;

R^2, R^4, R^3, and R^5 each independently is $-C_{0-6}$alkyl or $-C_{0-6}$alkyl–phenyl, optionally substituted with 1-6 independent halogen, –CN, NO_2, $-C_{1-6}$alkyl, $-OR^6$, $-NR^6R^7$, $-C(=NR^6)NR^7R^8$, $-N(-NR^{88}R^6)NR^7R^8$, $-NR^6COR^7$, $-NR^6CO_2R^7$, $-NR^6SO_2R^{88}$, $-NR^6CONR^7R^8$, $-SR^{88}$, $-SOR^{88}$, $-SO_2R^{88}$, $-SO_2NR^6R^7$, $-COR^6$, $-CO_2R^6$, $-CONR^6R^7$, $-C(=NR^6)R^7$, or $-C(=NOR^6)R^7$ substituents;

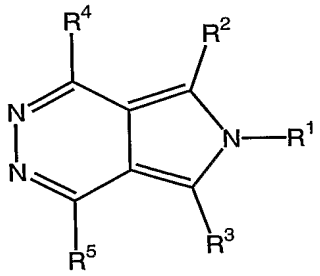
R^6, R^7, R^8, and R^{88} each independently is $-C_{0-6}$alkyl, $-C_{3-7}$cycloalkyl, heteroaryl, or aryl; optionally substituted with 1-5 independent halogen, -CN, $-C_{1-6}$alkyl, $-O(C_{0-6}$alkyl), $-O(C_{3-7}$cycloalkyl), -O(aryl), $-N(C_{0-6}$alkyl)(C_{0-6}alkyl), $-N(C_{0-6}$alkyl)(C_{3-7}cycloalkyl), or $-N(C_{0-6}$alkyl)(aryl) substituents; and

provided that the compound is not selected from the following table:



In another aspect, this invention is directed to a compound represented by Formula (I):



(I)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is $-C_{0-6}$alkyl–aryl, $-C_{0-6}$alkyl–heteroaryl, $-C_{0-6}$alkyl–C_{3-6}cycloalkyl, or $-C_{0-6}$alkyl–heteroC_{3-7}cycloalkyl, optionally substituted with 1-6 independent halogen, –CN, NO_2, $-C_{1-6}$alkyl, $-C_{0-6}$alkyl–C_{3-6}cycloalkyl, $-C_{0-6}$alkyl–heteroC_{3-7}cycloalkyl, $-OR^6$, $-NR^6R^7$, $-C(=NR^6)NR^7R^8$, $-N(-NR^{88}R^6)NR^7R^8$, $-NR^6COR^7$, $-NR^6CO_2R^7$, $-NR^6SO_2R^{88}$, $-NR^6CONR^7R^8$,

-SR^{88}, -SOR^{88}, –SO_2R^{88}, –$SO_2NR^6R^7$, -COR^6, -CO_2R^6, –$CONR^6R^7$, -$C(=NR^6)R^7$, or -$C(=NOR^6)R^7$ substituents;

R^2, R^4, R^3, and R^5 each independently is –C_{0-6}alkyl, –C_{0-6}alkyl–aryl, –C_{0-6}alkyl–heteroaryl, –C_{0-6}alkyl–C_{3-6}cycloalkyl, or –C_{0-6}alkyl–heteroC_{3-7}cycloalkyl, optionally substituted with 1-6 independent halogen, –CN, NO_2, -C_{1-6}alkyl, –OR^6, –NR^6R^7, –$C(=NR^6)NR^7R^8$, -$N(-NR^{88}R^6)NR^7R^8$, –NR^6COR^7, -$NR^6CO_2R^7$, -$NR^6SO_2R^{88}$, –$NR^6CONR^7R^8$, -SR^{88}, -SOR^{88}, –SO_2R^{88}, -$SO_2NR^6R^7$, -COR^6, -CO_2R^6, –$CONR^6R^7$, -$C(=NR^6)R^7$, or -$C(=NOR^6)R^7$ substituents;

R^6, R^7, R^8, and R^{88} each independently is –C_{0-6}alkyl, –C_{3-7}cycloalkyl, heteroaryl, or aryl; optionally substituted with 1-5 independent halogen, -CN, –C_{1-6}alkyl, –O(C_{0-6}alkyl), –O(C_{3-7}cycloalkyl), -O(aryl), –N(C_{0-6}alkyl)(C_{0-6}alkyl), –N(C_{0-6}alkyl)(C_{3-7}cycloalkyl), or -N(C_{0-6}alkyl)(aryl) substituents; provided that the compound is not

6-methyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

1,4,5,7-tetramethyl-6-phenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

1,4,5-trimethyl-6,7-diphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

5,7-dimethyl-1,4,6-triphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

5-methyl-1,4,6,7-tetraphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

1,4-bis-(4-methoxy-phenyl)-5,7-dimethyl-6-phenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

1,4-bis-(4-methoxy-phenyl)-5-methyl-6,7-diphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

1,4-diethyl-5,7-dimethyl-6-phenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

N-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-benzamide,

1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-ylamine picrate,

1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-ylamine,

5,7-dimethyl-6-phenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

5,7-dimethyl-2-phenacyl-6*H*-pyrrolo[3,4-*d*]pyridazinium bromide,

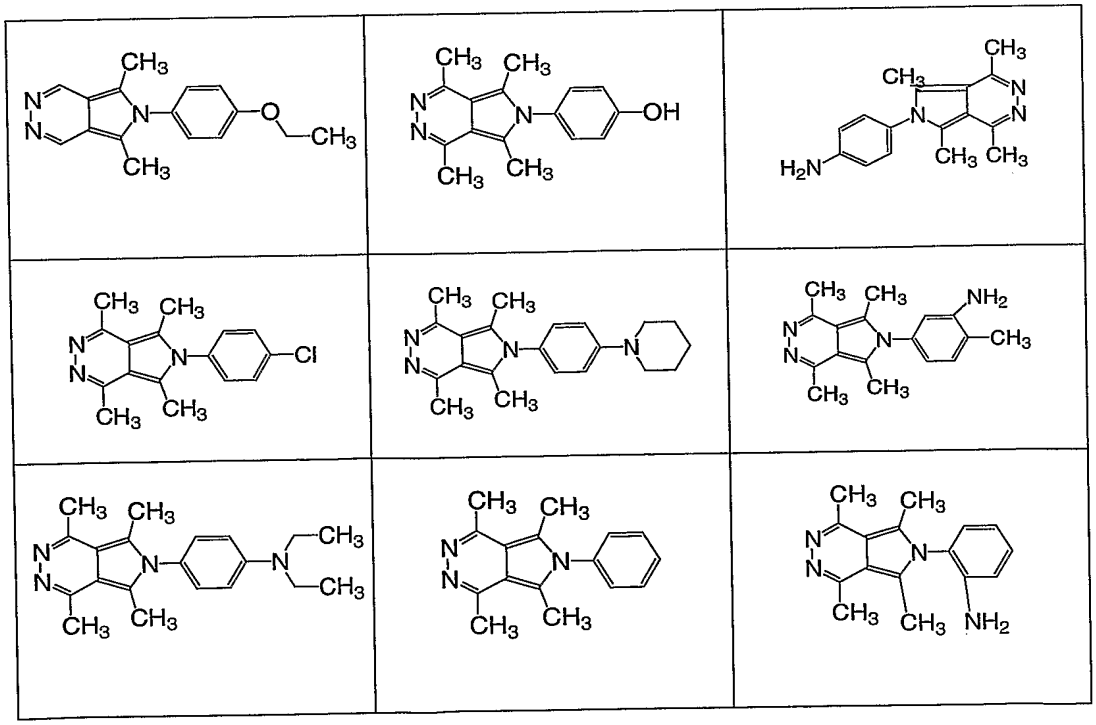
2-(2-methoxycarbonylvinyl)-5,7-dimethyl-6*H*-pyrrolo[3,4-*d*]pyridazinium tetrafloroborate

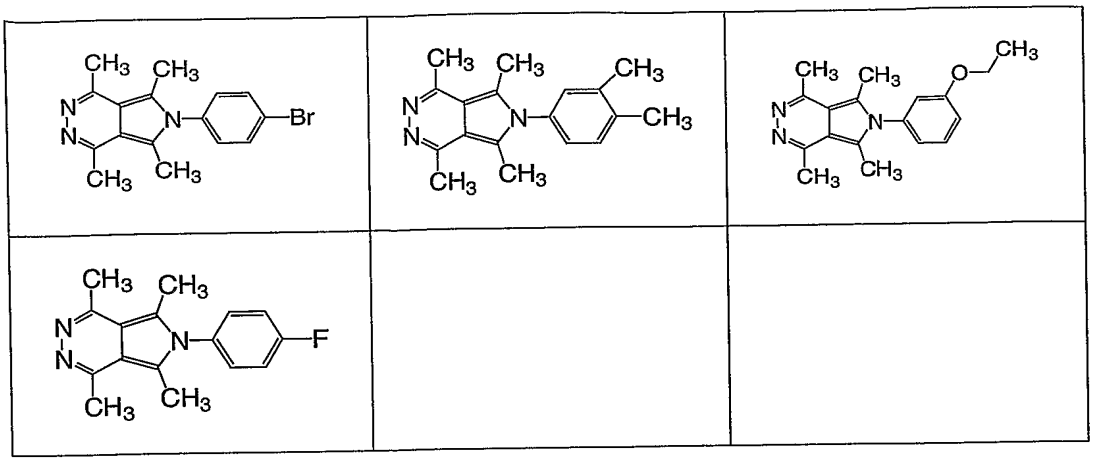
5,7-diphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

5,6,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

1,4-diphenyl-7,8,9,10-tetrahydro-pyridazino[4,5-*a*]indolizine,
5-methyl-1,4-diphenyl-7,8,9,10-tetrahydro-pyridazino[4,5-*a*]indolizine,
6-benzyl-1,4-diphenyl-5-p-tolyl-6*H*-pyrrolo[3,4-*d*]pyridazine,
6-benzyl-5-(2-chloro-phenyl)-1,4-diphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,
1,4,5,6,7-pentaphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,
6,7,10,11-tetraphenyl-pyridazino[4',5':3,4]pyrrolo[1,2-*a*]quinoxaline,
11-(4-nitro-phenyl)-6,7,10-triphenyl-pyridazino[4'.5':3,4]pyrrolo[1,2-*a*]quinoxaline,
6-benzyl-1,4,5-triphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,
9,12-diphenyl-pyridazino[4',5':3,4]pyrrolo[2,1-*a*]isoquinoline,
5-methylsulfanyl-1,4,6,7-tetraphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,
1,4,6,7-tetraphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine-5-carboxylic acid ethyl ester,
7,10-diphenyl-pyridazino[4',5':3,4]pyrrolo[1,2-*a*]quinoline,
11,14-diphenyl-pyridazino[4',5':3,4]pyrrolo[1,2-*f*]phenanthridine,
1-oxo-7-oxy-6b,11b-dihydro(pyridazino[4',5'-c]-pyrrolo)[2.1-c]benzoxazine-1,4,
10-methyl-1,4-diphenyl-8,9-dihydro-7H-benzo(ef)pyridazino[4,5-a]cycl[3.3.2]azine,
11-methyl-1,4-diphenyl-7,8,9,10-tetrahydrocyclohepta(ef)pyridazino[4,5-a]cycl[3.3.2]azine,
1,4-dichloro-5,6,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine,
1-chloro-4-ethoxy-5,6,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine,
1-chloro-5,6,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazinium chloride,
1-ethoxy-2,5,6,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazinium tetrafluoroborate,
1-ethoxy-5,6,7-trimethyl-2*H*,6*H*-pyrrolo[3,4-*d*]pyridazinium tetrafluoroborate,
1-ethoxy-3-ethyl-5,6,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazinium tetrafluoroborate,
1-ethoxy-5,6,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine,
5-cyano-1,4-dimethylpyridazino[4,5-*a*]indolizine,
1,4-dimethyl-6-phenyl-2,3,8a-triaza-fluorene-9-carbonitrile,
6-benzolyl-1,4-dimethyl-2,3,8a-triaza-fluorene-9-carbonitrile,

6-benzyl-1,4-diphenyl-2,3,8a-triaza-fluorene-9-carbonitrile,
1,4,6-trimethyl-2,3,8a-triaza-fluorene-9-carbonitrile,
5-cyano-1,4-diphenylpyridazino[4,5-*a*]indolizine,
6-methyl-1,4-diphenyl-2,3,8a-triaza-fluorene-9-carbonitrile,
6-benzoyl-1,4-diphenyl-2,3,8a-triaza-fluorene-9-carbonitrile,
1,4,6-triphenyl-2,3,8a-triaza-fluorene-9-carbonitrile,
5,7-dimethyl-1,4-diphenyl-2,3,8a-triaza-fluorene-9-carbonitrile,
9,12-diphenyl-pyridazino[4',5':3,4]pyrrolo[2,1-*a*]isoquinoline-8-carbonitrile,
dimethyl 3,12,13,17-tetramethyl-7^2,7^3-diazabenzo[g]porphyrin-2,18-dipropionate,
5,6-dihydro-2,3-dimethoxypyridazino[4',5':3,4]pyrrolo[2,1-*a*]isochinolin-9-ol,
5,6-dihydro-2,3-dimethoxypyridazino[4',5':3,4]pyrrolo[2,1-*a*]isochinolin-9-ol-hydrochloride,
3-methyl-6,9-diphenylthiazolo[3',2':1,2]pyrrolo[3,4-*d*]pyridine, or
1,4-diphenylpyridazino[4',5':3,4]pyrrolo[2,1-*b*]benzothiazole;
and the compound is not selected from the following table:





As used herein, "alkyl" as well as other groups having the prefix "alk" such as, for example, alkoxy, alkanoyl, alkenyl, alkynyl and the like, means carbon chains which may be linear or branched or combinations thereof. Examples of alkyl groups include methyl, ethyl, propyl, isopropyl, butyl, sec- and tert-butyl, pentyl, hexyl, heptyl and the like. "Alkenyl", "alkynyl" and other like terms include carbon chains containing at least one unsaturated C-C bond.

The term "cycloalkyl" means carbocycles containing no heteroatoms, and includes mono-, bi- and tricyclic saturated carbocycles, as well as fused ring systems. Such fused ring systems can include one ring that is partially or fully unsaturated such as a benzene ring to form fused ring systems such as benzofused carbocycles. Cycloalkyl includes such fused ring systems as spirofused ring systems. Examples of cycloalkyl include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, decahydronaphthalene, adamantane, indanyl, indenyl, fluorenyl, 1,2,3,4-tetrahydronaphalene and the like. Similarly, "cycloalkenyl" means carbocycles containing no heteroatoms and at least one non-aromatic C-C double bond, and include mono-, bi- and tricyclic partially saturated carbocycles, as well as benzofused cycloalkenes. Examples of cycloalkenyl include cyclohexenyl, indenyl, and the like.

The term "aryl" means an aromatic substituent which is a single ring or multiple rings fused together. When formed of multiple rings, at least one of the constituent rings is aromatic. The preferred aryl substituents are phenyl and naphthyl groups.

The term "cycloalkyloxy" unless specifically stated otherwise includes a cycloalkyl group connected by a short C_{1-2}alkyl length to the oxy connecting atom.

The term "C_{0-6}alkyl" includes alkyls containing 6, 5, 4, 3, 2, 1, or no carbon atoms. An alkyl with no carbon atoms is a hydrogen atom substituent when the alkyl is a terminal group and is a direct bond when the alkyl is a bridging group.

The term "hetero" unless specifically stated otherwise includes one or more O, S, or N atoms. For example, heterocycloalkyl and heteroaryl include ring systems that contain one or more O, S, or N atoms in the ring, including mixtures of such atoms. The hetero atoms replace ring carbon atoms. Thus, for example, a heterocycloC_5alkyl is a five-member ring containing from 4 to no carbon atoms. Examples of heteroaryls include pyridinyl, quinolinyl, isoquinolinyl, pyridazinyl, pyrimidinyl, pyrazinyl, quinoxalinyl, furyl, benzofuryl, dibenzofuryl, thienyl, benzthienyl, pyrrolyl, indolyl, pyrazolyl, indazolyl, oxazolyl, benzoxazolyl, isoxazolyl, thiazolyl, benzothiazolyl, isothiazolyl, imidazolyl, benzimidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, and tetrazolyl. Examples of heterocycloalkyls include azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, tetrahydrofuranyl, imidazolinyl, pyrolidin-2-one, piperidin-2-one, and thiomorpholinyl.

The term "heteroC_{0-4}alkyl" means a heteroalkyl containing 3, 2, 1, or no carbon atoms. However, at least one heteroatom must be present. Thus, as an example, a heteroC_{0-4}alkyl having no carbon atoms but one N atom would be a -NH– if a bridging group and a $-NH_2$ if a terminal group. Analogous bridging or terminal groups are clear for an O or S heteroatom.

The term "amine" unless specifically stated otherwise includes primary, secondary and tertiary amines substituted with C_{0-6}alkyl.

The term "carbonyl" unless specifically stated otherwise includes a C_{0-6}alkyl substituent group when the carbonyl is terminal.

The term "halogen" includes fluorine, chlorine, bromine and iodine atoms.

The term "optionally substituted" is intended to include both substituted and unsubstituted. Thus, for example, optionally substituted aryl could represent a pentafluorophenyl or a phenyl ring. Further, optionally substituted multiple moieties such as, for example, alkylaryl are intended to mean that the aryl and the alkyl groups are optionally substituted. If only one of the multiple moieties is optionally substituted then it will be specifically recited such as "an alkylaryl, the aryl optionally substituted with halogen or hydroxyl."

Compounds described herein contain one or more double bonds and may thus give rise to cis/trans isomers as well as other conformational isomers. The present invention includes all such possible isomers as well as mixtures of such isomers.

Compounds described herein can contain one or more asymmetric centers and may thus give rise to diastereomers and optical isomers. The present invention includes the use of all such possible diastereomers as well as their racemic mixtures, their substantially pure resolved enantiomers, all possible geometric isomers, and pharmaceutically acceptable salts thereof. The above Formula I is shown without a definitive stereochemistry at certain positions. The present invention includes the use of all stereoisomers of Formula I and pharmaceutically acceptable salts thereof. Further, mixtures of stereoisomers as well as isolated specific stereoisomers are also included. During the course of the synthetic procedures used to prepare such compounds, or in using racemization or epimerization procedures known to those skilled in the art, the products of such procedures can be a mixture of stereoisomers.

The term "pharmaceutically acceptable salts" refers to salts prepared from pharmaceutically acceptable non-toxic bases or acids. When the compound used in the present invention is acidic, its corresponding salt can be conveniently prepared from pharmaceutically acceptable non-toxic bases, including inorganic bases and organic bases. Salts derived from such inorganic bases include aluminum, ammonium, calcium, copper (ic and ous), ferric, ferrous, lithium, magnesium, manganese (ic and ous), potassium, sodium, zinc and the like salts. Particularly preferred are the ammonium, calcium, magnesium, potassium and sodium salts. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines, as well as cyclic amines and substituted amines such as naturally occurring and synthesized substituted amines. Other pharmaceutically acceptable organic non-toxic bases from which salts can be formed include ion exchange resins such as, for example, arginine, betaine, caffeine, choline, N,N'-dibenzylethylenediamine, diethylamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethylmorpholine, N-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, lysine, methylglucamine, morpholine, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine, tromethamine and the like.

When the compound used in the present invention is basic, its corresponding salt can be conveniently prepared from pharmaceutically acceptable non-toxic acids, including inorganic and organic acids. Such acids include, for example, acetic, benzenesulfonic, benzoic, camphorsulfonic, citric, ethanesulfonic, fumaric, gluconic, glutamic, hydrobromic, hydrochloric, isethionic, lactic, maleic, malic, mandelic, methanesulfonic, mucic, nitric, pamoic, pantothenic, phosphoric, succinic, sulfuric, tartaric, p-toluenesulfonic acid and the like. Particularly preferred are citric, hydrobromic, hydrochloric, maleic, phosphoric, sulfuric, and tartaric acids.

The pharmaceutical compositions used of 2H-pyrrolo[3,4-c]pyridazine compounds of the present invention comprise a compound represented by Formula I (or pharmaceutically acceptable salts thereof) as an active ingredient, a pharmaceutically acceptable carrier and optionally other therapeutic ingredients or adjuvants. Such additional therapeutic ingredients include, for example, i) opiate agonists or antagonists, ii) calcium channel antagonists, iii) 5HT receptor agonists or antagonists iv) sodium channel antagonists, v) NMDA receptor agonists or antagonists, vi) COX-2 selective inhibitors, vii) NK1 antagonists, viii) non-steroidal anti-inflammatory drugs ("NSAID"), ix) GABA-A receptor modulators, x) dopamine agonists or antagonists, xi) selective serotonin reuptake inhibitors ("SSRI") and/or selective serotonin and norepinephrine reuptake inhibitors ("SSNRI"), xii) tricyclic antidepressant drugs, xiv) norepinephrine modulators, xv) L-DOPA, xvi) buspirone, xvii) lithium, xviii) valproate, ixx) neurontin (gabapentin), xx) olanzapine, xxi) nicotinic agonists or antagonists including nicotine, xxii) muscarinic agonists or antagonists, xxiii) heroin substituting drugs such as methadone, levo-alpha-acetylmethadol, buprenorphine and naltrexone, and xxiv) disulfiram and acamprosate. The compositions include compositions suitable for oral, rectal, topical, and parenteral (including subcutaneous, intramuscular, and intravenous) administration, although the most suitable route in any given case will depend on the particular host, and nature and severity of the conditions for which the active ingredient is being administered. The pharmaceutical compositions may be conveniently presented in unit dosage form and prepared by any of the methods well known in the art of pharmacy.

Creams, ointments, jellies, solutions, or suspensions containing the compound of Formula I can be employed for topical use. Mouth washes and gargles are included within the scope of topical use for the purposes of this invention.

Dosage levels from about 0.01mg/kg to about 140mg/kg of body weight per day are useful in the treatment of psychiatric and mood disorders such as, for example, schizophrenia, anxiety, depression, panic, bipolar disorders, and circadian disorders, as well as being useful in the treatment of pain which are responsive to calcium channel modulation, or alternatively about 0.5mg to about 7g per patient per day. For example, schizophrenia, anxiety, depression, and panic may be effectively treated by the administration of from about 0.01mg to 75mg of the compound per kilogram of body weight per day, or alternatively about 0.5mg to about 3.5g per patient per day. Pain may be effectively treated by the administration of from about 0.01mg to 125mg of the compound per kilogram of body weight per day, or alternatively about 0.5mg to about 5.5g per patient per day. Further, it is understood that the calcium channel modulating compounds of this invention can be administered at prophylactically effective dosage levels to prevent the above-recited conditions.

The amount of active ingredient that may be combined with the carrier materials to produce a single dosage form will vary depending upon the host treated and the particular mode of administration. For example, a formulation intended for the oral administration to humans may conveniently contain from about 0.5mg to about 5g of active agent, compounded with an appropriate and convenient amount of carrier material which may vary from about 5 to about 95 percent of the total composition. Unit dosage forms will generally contain between from about 1mg to about 1000mg of the active ingredient, typically 25mg, 50mg, 100mg, 200mg, 300mg, 400mg, 500mg, 600mg, 800mg or 1000mg.

It is understood, however, that the specific dose level for any particular patient will depend upon a variety of factors including the age, body weight, general health, sex, diet, time of administration, route of administration, rate of excretion, drug combination and the severity of the particular disease undergoing therapy.

In practice, the compounds used represented by Formula I, or pharmaceutically acceptable salts thereof, of this invention can be combined as the active ingredient in intimate admixture with a pharmaceutical carrier according to conventional pharmaceutical compounding techniques. The carrier may take a wide variety of forms depending on the form of preparation desired for administration, e.g., oral or parenteral (including intravenous). Thus, the pharmaceutical compositions used in the present invention can be presented as discrete units suitable for oral administration such as capsules, cachets or tablets each containing a predetermined amount of the active ingredient. Further, the compositions can be presented as a

powder, as granules, as a solution, as a suspension in an aqueous liquid, as a non-aqueous liquid, as an oil-in-water emulsion or as a water-in-oil liquid emulsion. In addition to the common dosage forms set out above, the compound represented by Formula I, or pharmaceutically acceptable salts thereof, may also be administered by controlled release means and/or delivery devices. The compositions may be prepared by any of the methods of pharmacy. In general, such methods include a step of bringing into association the active ingredient with the carrier that constitutes one or more necessary ingredients. In general, the compositions are prepared by uniformly and intimately admixing the active ingredient with liquid carriers or finely divided solid carriers or both. The product can then be conveniently shaped into the desired presentation.

Thus, the pharmaceutical compositions used in this invention may include a pharmaceutically acceptable carrier and a compound or a pharmaceutically acceptable salt of Formula I. The compounds of Formula I, or pharmaceutically acceptable salts thereof, can also be included in pharmaceutical compositions in combination with one or more other therapeutically active compounds.

The pharmaceutical carrier employed can be, for example, a solid, liquid, or gas. Examples of solid carriers include lactose, terra alba, sucrose, talc, gelatin, agar, pectin, acacia, magnesium stearate, and stearic acid. Examples of liquid carriers are sugar syrup, peanut oil, olive oil, and water. Examples of gaseous carriers include carbon dioxide and nitrogen.

In preparing the compositions for oral dosage form, any convenient pharmaceutical media may be employed. For example, water, glycols, oils, alcohols, flavoring agents, preservatives, coloring agents and the like may be used to form oral liquid preparations such as suspensions, elixirs and solutions; while carriers such as starches, sugars, microcrystalline cellulose, diluents, granulating agents, lubricants, binders, disintegrating agents, and the like may be used to form oral solid preparations such as powders, capsules and tablets. Because of their ease of administration, tablets and capsules are the preferred oral dosage units whereby solid pharmaceutical carriers are employed. Optionally, tablets may be coated by standard aqueous or nonaqueous techniques

A tablet containing the composition of this invention may be prepared by compression or molding, optionally with one or more accessory ingredients or adjuvants. Compressed tablets may be prepared by compressing, in a suitable machine, the active ingredient in a free-flowing form such as powder or granules,

optionally mixed with a binder, lubricant, inert diluent, surface active or dispersing agent. Molded tablets may be made by molding in a suitable machine, a mixture of the powdered compound moistened with an inert liquid diluent. Each tablet preferably contains from about 0.1mg to about 500mg of the active ingredient and each cachet or capsule preferably containing from about 0.1mg to about 500mg of the active ingredient. Thus, a tablet, cachet, or capsule conveniently contains 0.1mg, 1mg, 5mg, 25mg, 50mg, 100mg, 200mg, 300mg, 400mg, or 500mg of the active ingredient taken one or two tablets, cachets, or capsules, once, twice, or three times daily.

Pharmaceutical compositions used in the present invention suitable for parenteral administration may be prepared as solutions or suspensions of the active compounds in water. A suitable surfactant can be included such as, for example, hydroxypropylcellulose. Dispersions can also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof in oils. Further, a preservative can be included to prevent the detrimental growth of microorganisms.

Pharmaceutical compositions used in the present invention suitable for injectable use include sterile aqueous solutions or dispersions. Furthermore, the compositions can be in the form of sterile powders for the extemporaneous preparation of such sterile injectable solutions or dispersions. In all cases, the final injectable form must be sterile and must be effectively fluid for easy syringability. The pharmaceutical compositions must be stable under the conditions of manufacture and storage; thus, preferably should be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (e.g. glycerol, propylene glycol and liquid polyethylene glycol), vegetable oils, and suitable mixtures thereof.

Pharmaceutical compositions used in the present invention can be in a form suitable for topical use such as, for example, an aerosol, cream, ointment, lotion, dusting powder, or the like. Further, the compositions can be in a form suitable for use in transdermal devices. These formulations may be prepared, utilizing a compound represented by Formula I of this invention, or pharmaceutically acceptable salts thereof, via conventional processing methods. As an example, a cream or ointment is prepared by mixing hydrophilic material and water, together with about 5 wt% to about 10 wt% of the compound, to produce a cream or ointment having a desired consistency.

Pharmaceutical compositions used in this invention can be in a form suitable for rectal administration wherein the carrier is a solid. It is preferable that the mixture forms unit dose suppositories. Suitable carriers include cocoa butter and other materials commonly used in the art. The suppositories may be conveniently formed by first admixing the composition with the softened or melted carrier(s) followed by chilling and shaping in moulds.

In addition to the aforementioned carrier ingredients, the pharmaceutical formulations described above may include, as appropriate, one or more additional carrier ingredients such as diluents, buffers, flavoring agents, binders, surface-active agents, thickeners, lubricants, preservatives (including anti-oxidants) and the like. Furthermore, other adjuvants can be included to render the formulation isotonic with the blood of the intended recipient. Compositions containing a compound described by Formula I, or pharmaceutically acceptable salts thereof, may also be prepared in powder or liquid concentrate form.

The compounds and pharmaceutical compositions used in this invention have been found to exhibit biological activity as calcium channel ligands. Accordingly, another aspect of the invention is the treatment in mammals of, for example, schizophrenia, anxiety, depression, panic, bipolar disorders, circadian rhythm and sleep disorders, pain, Parkinson's disease, cognitive dysfunction, epilepsy, drug addiction, drug abuse and drug withdrawal – maladies that are amenable to amelioration through modulation of the calcium channel – by the administration of an effective amount of the compounds of this invention. The term "mammals" includes humans, as well as other animals such as, for example, dogs, cats, horses, pigs, and cattle. Accordingly, it is understood that the treatment of mammals other than humans is the treatment of clinical correlating afflictions to those above recited examples that are human afflictions.

Further, as described above, the compound used in this invention can be utilized in combination with other therapeutic compounds. In particular, the combinations of the clacium channel modulating compound used in this invention can be advantageously used in combination with i) opiate agonists or antagonists, ii) mGluR5 antagonists, iii) 5HT receptor agonists or antagonists iv) sodium channel antagonists, v) NMDA receptor agonists or antagonists, vi) COX-2 selective inhibitors, vii) NK1 antagonists, viii) non-steroidal anti-inflammatory drugs ("NSAID"), ix) GABA-A receptor modulators, x) dopamine agonists or antagonists, xi) selective serotonin reuptake inhibitors ("SSRI") and/or selective serotonin and

norepinephrine reuptake inhibitors ("SSNRI"), xii) tricyclic antidepressant drugs, xiii) norepinephrine modulators, xiv) L-DOPA, xv) buspirone, xvi) lithium, xvii) valproate, xviii) neurontin (gabapentin), xix) olanzapine, xx) nicotinic agonists or antagonists including nicotine, xxi) muscarinic agonists or antagonists, xxii) heroin substituting drugs such as methadone, levo-alpha-acetylmethadol, buprenorphine and naltrexone, and xxiii) disulfiram and acamprosate.

The abbreviations used herein have the following tabulated meanings. Abbreviations not tabulated below have their meanings as commonly used unless specifically stated otherwise.

Ac	acetyl
AIBN	2,2'-azobis(isobutyronitrile)
BINAP	1,1'-bi-2-naphthol
Bn	benzyl
CAMP	cyclic adenosine-3',5'-monophosphate
DAST	(diethylamino)sulfur trifluoride
DEAD	diethyl azodicarboxylate
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DIBAL	diisobutylaluminum hydride
DMAP	4-(dimethylamino)pyridine
DMF	N,N-dimethylformamide
Dppf	1,1'-bis(diphenylphosphino)-ferrocene
EDCI	1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride
Et_3N	triethylamine
GST	glutathione transferase
HMDS	hexamethyldisilazide
LDA	lithium diisopropylamide
m-CPBA	metachloroperbenzoic acid
MMPP	monoperoxyphthalic acid
MPPM	monoperoxyphthalic acid, magnesium salt $6H_2O$
Ms	methanesulfonyl = mesyl = SO_2Me
Ms0	methanesulfonate = mesylate

NBS	N-bromo succinimide
NSAID	non-steroidal anti-inflammatory drug
o-Tol	ortho-tolyl
OXONE®	$2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$
PCC	pyridinium chlorochromate
$Pd_2(dba)_3$	Bis(dibenzylideneacetone) palladium(0)
PDC	pyridinium dichromate
PDE	Phosphodiesterase
Ph	Phenyl
Phe	Benzenediyl
PMB	para-methoxybenzyl
Pye	Pyridinediyl
r.t.	room temperature
Rac.	Racemic
SAM	aminosulfonyl or sulfonamide or SO_2NH_2
SEM	2-(trimethylsilyl)ethoxymethoxy
SPA	scintillation proximity assay
TBAF	tetra-n-butylammonium fluoride
Th	2- or 3-thienyl
TFA	trifluoroacetic acid
TFAA	trifluoroacetic acid anhydride
THF	Tetrahydrofuran
Thi	Thiophenediyl
TLC	thin layer chromatography
TMS-CN	trimethylsilyl cyanide
TMSI	trimethylsilyl iodide
Tz	1H (or 2H)-tetrazol-5-yl
XANTPHOS	4,5-Bis-diphenylphosphanyl-9,9-dimethyl-9H-xanthene
C_3H_5	Allyl

ALKYL GROUP ABBREVIATIONS

Me	=	Methyl
Et	=	ethyl
n-Pr	=	normal propyl
i-Pr	=	isopropyl
n-Bu	=	normal butyl
i-Bu	=	isobutyl
s-Bu	=	secondary butyl
t-Bu	=	tertiary butyl
c-Pr	=	cyclopropyl
c-Bu	=	cyclobutyl
c-Pen	=	cyclopentyl
c-Hex	=	cyclohexyl

ASSAYS DEMONSTRATING BIOLOGICAL ACTIVITY

The compounds of this invention were tested by the following assays.

Membrane Preparation:

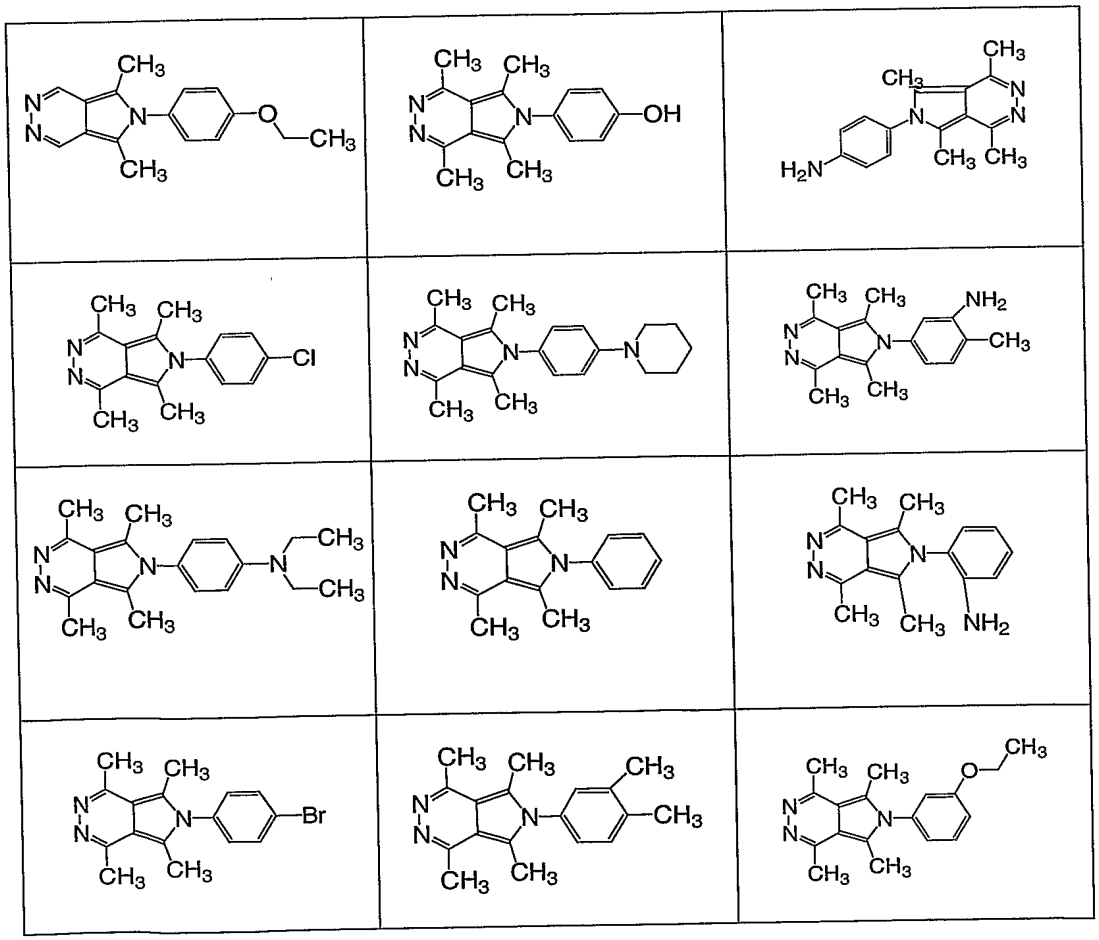
A710 (HEK293 co-expressing α1b, α2δ, β3) cultured in T250 flask were harvested and washed once with buffer A (20mM HEPES 10mM EDTA pH=7.4). The pellet was homogenized in buffer A using a Polytron for 20s. After centrifugation for 10min, the resulting pellet was washed once with the same buffer and twice with buffer B (20mM HEPES 0.1mM EDTA pH=7.4). The final pellet was resuspended in the same buffer and aliquoted and stored at –70°C. Protein contents was measured by the Biorad D C method with bovine serum albumin used as standard.

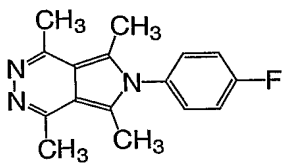
[^{3}H]-GABApentin binding:

After thawing, the membranes were washed one time with buffer C (50mM TRIS pH=7.1) and resuspended in ice cold assay buffer (20mM HEPES pH=7.4), to have a final protein concentration of 50μg of protein/well. For the competitive binding experiments, the membranes were incubated with 7nM [^{3}H]-

GABApentin for 1h at rt in the absence or the presence of at least 11 concentrations of the compounds to be tested. The non-specific binding was measured in the presence of 100μM GABApentin. At the end of the incubation, the suspension was filtered onto 96 well Whatmann GF/B filter plate (Packard) and washed 3 times with ice-cold assay buffer. The plate was dried and 50μL of microscint 20 (Packard) was added in each well. The plate was sealed and was counted using a Packard Topcount. The plate was counted (2min) in normal cpm count mode and transforms in DPM with a constant quench correction.

The compounds of this invention displayed efficacy in the above model by IC_{50} values of less than 10μM. The compounds the following table, however, gave IC_{50} values of more than 10μM:



Spinal Nerve Ligation Model (Chung Model):

The spinal nerve ligation model of neuropathic pain was used to assess the effects of test compounds on nerve injury-induced tactile allodynia (S.H. Kim and J.M. Chung, *Pain* 50:355-363(1992)). Male Sprague Dawley rats (175-200g) received unilateral tight ligation of the left L5/L6 spinal nerves distal to the dorsal root ganglion using 4-0 silk suture. Behavioral nociceptive testing occurred 7-14 days following spinal nerve ligation by placing the rats in chambers on a wire mesh. Rats were tested for tactile allodynia (decreased hindpaw withdrawal threshold to non-noxious punctate stimulation) by applying a series of calibrated von Frey filaments to the plantar aspect of the left hindpaw ipsilateral to the site of nerve injury. The mean 50% hindpaw withdrawal threshold (g.) was determined using the Dixon "up-down" non-parametric test (Chaplan et al., *J. Neurosci. Methods*, 53:55-63(1994)). Rats that displayed a pre-drug withdrawal threshold >4g were not considered allodynic and were excluded from the study. Following determination of pre-drug withdrawal thresholds, rats received either an i.p. or p.o. injection of test compound. The effect of the test compound on tactile allodynia was determined over time by measuring hindpaw withdrawal thresholds 30, 60, 90, 120min post-injection. In above model, EXAMPLE 1 produced a 65% effect after i.p. dosing at 30 mg/kg, EXAMPLE 50 produced a 100% effect after i.p. dosing at 20 mg/kg, EXAMPLE 115 produced a 60% effect after i.p. dosing at 30 mg/kg i.p.

The examples that follow are intended as an illustration of certain preferred embodiments of the invention and no limitation of the invention is implied.

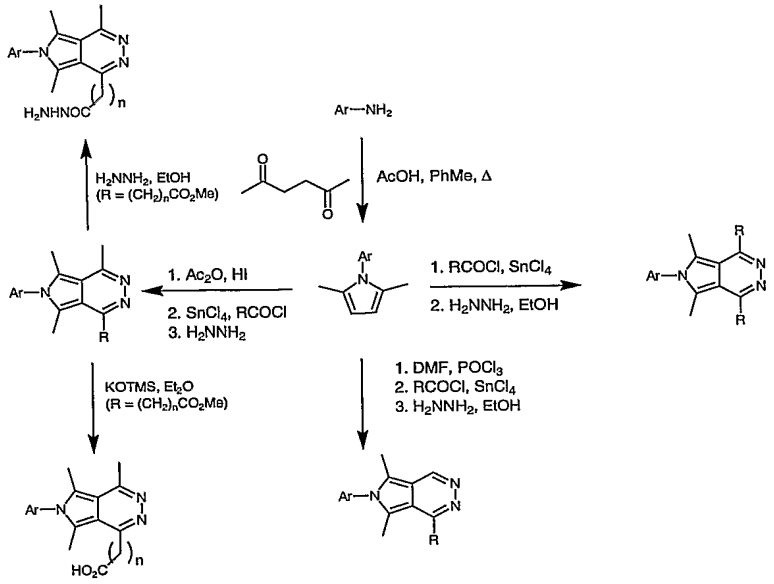
Unless specifically stated otherwise, the experimental procedures were performed under the following conditions. All operations were carried out at room or ambient temperature - that is, at a temperature in the range of 18-25°C. Evaporation of solvent was carried out using a rotary evaporator under reduced pressure (600-4000pascals: 4.5-30mm Hg) with a bath temperature of up to 60°C. The course of reactions was followed by thin layer chromatography (TLC) and reaction times are

given for illustration only. Melting points are uncorrected and 'd' indicates decomposition. The melting points given are those obtained for the materials prepared as described. Polymorphism may result in isolation of materials with different melting points in some preparations. The structure and purity of all final products were assured by at least one of the following techniques: TLC, mass spectrometry, nuclear magnetic resonance (NMR) spectrometry or microanalytical data. When given, yields are for illustration only. When given, NMR data is in the form of delta (δ) values for major diagnostic protons, given in parts per million (ppm) relative to tetramethylsilane (TMS) as internal standard, determined at 300MHz, 400MHz or 500MHz using the indicated solvent. Conventional abbreviations used for signal shape are: s. singlet; d. doublet; t. triplet; m. multiplet; br. broad; etc. In addition, "Ar" signifies an aromatic signal. Chemical symbols have their usual meanings; the following abbreviations are used: v (volume), w (weight), b.p. (boiling point), m.p. (melting point), L (liter(s)), mL (milliliters), g (gram(s)), mg (milligrams(s)), mol (moles), mmol (millimoles), eq (equivalent(s)).

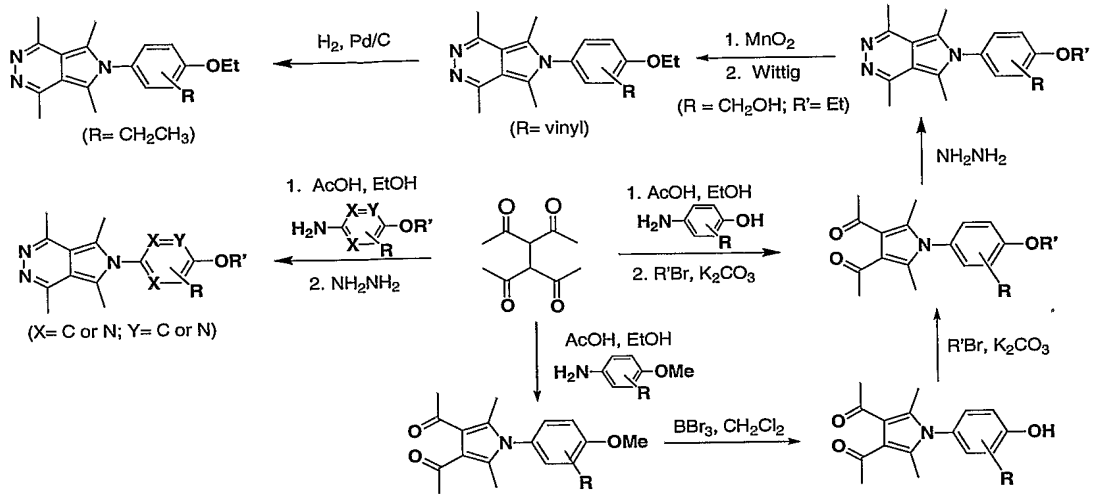
Methods of Synthesis

Compounds of the present invention can be prepared according to the following methods. The substituents are the same as in Formula **I** except where defined otherwise.

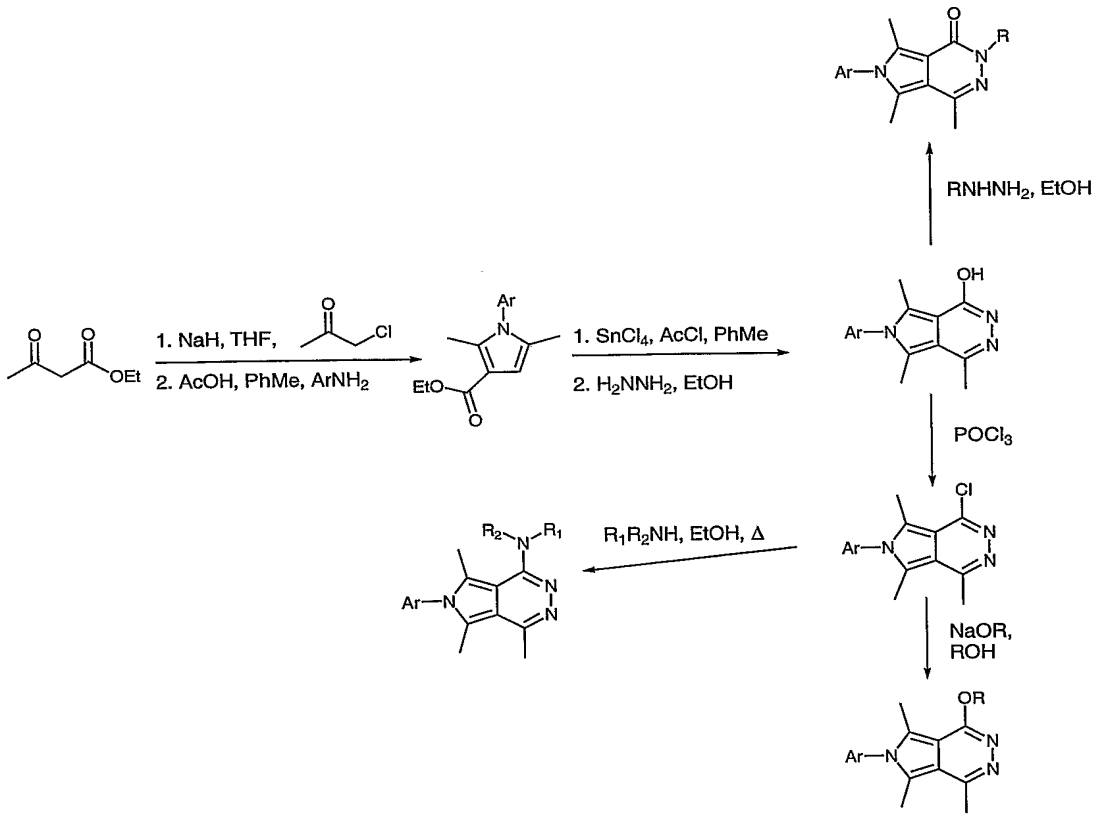
EXAMPLES 1-47:



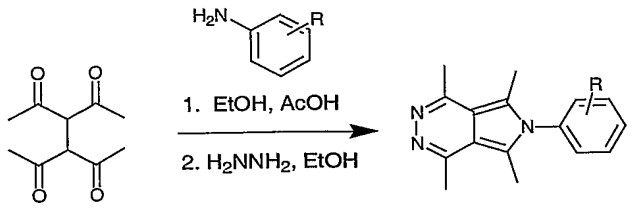
EXAMPLES 48-84:



EXAMPLES 85-370:

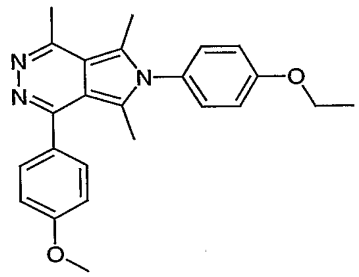


EXAMPLE 371:



EXAMPLE 1

6-(4-ethoxyphenyl)-1-(4-methoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



To a solution of acetonyl acetone (11.7mL, 100mmol) and toluene (750mL) was added *p*-phenetidine (12.9mL, 100mmol) and glacial acetic acid (1mL). The mixture was heated at reflux overnight. After cooling to rt, the mixture was concentrated *in vacuo* and purified by column chromatography on silica gel (15% EtOAc/hexanes) to give 2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole as a pale yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.13 – 7.10 (m, 2H), 6.97 – 6.94 (m, 2H), 5.88 (br s, 2H), 4.08 (q, 2H), 2.02 (s, 6H), 1.46 (t, 3H); MS (ESI) 216 $(M + H)^+$.

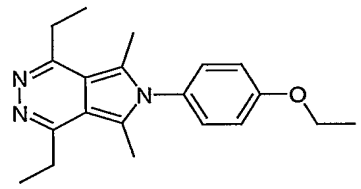
Acetic anhydride (8.5mL, 89mmol) and hydriodic acid (0.48mL, 6.3mmol) were added to 2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (8.0g, 37mmol) under nitrogen and the resulting mixture maintained at 100°C overnight. After cooling to rt, the mixture was diluted with 1N NaOH (200mL), extracted with EtOAc (2 x 200mL), and the combined extracts washed with brine (200mL), dried ($MgSO_4$), filtered, concentrated *in vacuo*, and purified by flash chromatography on silica gel (15% EtOAc/hexanes) to give 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole as a tan solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.08 – 7.04 (m, 2H), 6.99 – 6.96 (m, 2H),

6.30 (s, 1H), 4.08 (q, 2H), 2.41 (s, 3H), 2.29 (s, 3H), 1.97 (s, 3H), 1.45 (t, 3H); MS (ESI) 258 $(M + H)^+$.

To a solution of 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (200mg, 0.78mmol) and toluene (4mL) at 0°C was added dropwise $SnCl_4$ (0.94mL, 0.94mmol, 1.0M solution in CH_2Cl_2) and *p*-anisoyl chloride (160mg, 0.94mmol). The mixture was allowed to warm to rt and heated at 50°C overnight. After cooling to rt, the mixture was diluted with 1N NaOH (15mL), extracted with EtOAc (2 x 15mL), and the combined extracts washed with brine (15mL), dried ($MgSO_4$), filtered, concentrated *in vacuo*, and purified by flash chromatography (0 – 33% EtOAc/hexanes). The resulting residue was dissolved in EtOH (5mL) and hydrazine (0.5mL). The solution was stirred at 50°C overnight, cooled to rt, and concentrated *in vacuo* to give 6-(4-ethoxyphenyl)-1-(4-methoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a light yellow solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.57 – 7.54 (m, 2H), 7.12 – 7.09 (m, 2H), 7.05 – 7.03 (m, 2H), 6.99 – 6.97 (m, 2H), 4.11 (q, 2H), 3.85 (s, 3H), 2.90 (s, 3H), 2.49 (s, 3H), 1.94 (s, 3H), 1.47 (t, 3H); MS (ESI) 388 $(M + H)^+$.

EXAMPLE 2

1,4-diethyl-5,7-dimethyl-6-(4-ethoxyphenyl)-6*H*-pyrrolo[3,4-*d*]pyridazine

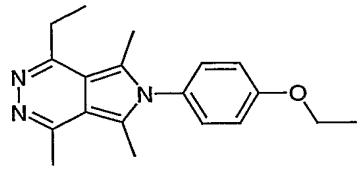


To a solution of 2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (**EXAMPLE 1**) (1.0g, 4.7mmol) and toluene (15mL) at 0°C was added dropwise $SnCl_4$ (4.7mL, 4.7mmol, 1.0M solution in CH_2Cl_2) and propionyl chloride (0.40mL, 4.7mmol). The mixture was warmed to rt and then heated at 50°C overnight. After cooling to rt, the mixture was quenched with 1N NaOH (50mL), extracted with EtOAc (2 x 50mL), the combined extracts washed with brine (50mL), dried ($MgSO_4$), filtered, concentrated *in vacuo*, and purified by flash chromatography on silica gel (0–25% EtOAc/hexanes). The resulting residue was dissolved in EtOH (10mL) and hydrazine (0.1mL). The resulting solution was maintained at 50°C overnight, cooled to rt, and concentrated *in vacuo* to give 1,4-diethyl-5,7-dimethyl-6-(4-ethoxyphenyl)-6*H*-pyrrolo[3,4-*d*]pyridazine as a light yellow solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.13 – 7.10 (m,

2H), 7.06 – 7.03 (m, 2H), 4.12 (q, 2H), 3.11 (q, 4H), 2.40 (s, 6H), 1.48 (t, 3H), 1.39 (t, 6H); MS (ESI) 324 $(M + H)^+$.

EXAMPLE 3

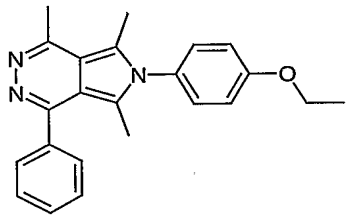
6-(4-ethoxyphenyl)-1-ethyl-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (200mg, 0.78mmol) and propionyl chloride (0.08mL, 0.94mmol) reacted to give 6-(4-ethoxyphenyl)-1-ethyl-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a light yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.13 – 7.11 (m, 2H), 7.08 – 7.05 (m, 2H), 4.13 (q, 2H), 3.15 (q, 2H), 2.85 (s, 3H), 2.45 (s, 3H), 2.42 (s, 3H), 1.49 (t, 3H), 1.40 (t, 3H); MS (ESI) 310 $(M + H)^+$.

EXAMPLE 4

6-(4-ethoxyphenyl)-1-phenyl-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



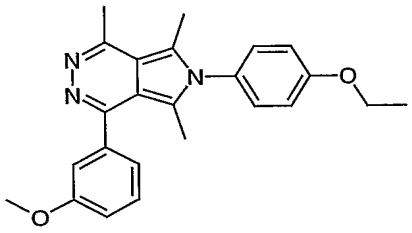
To a solution of 2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (**EXAMPLE 1**) (1.0g, 4.7mmol) and toluene (15mL) at 0°C was added dropwise $SnCl_4$ (4.7mL, 4.7mmol, 1.0M solution in CH_2Cl_2) and benzoyl chloride (0.54mL, 4.7mmol). The mixture was warmed to rt and heated at 50°C overnight. After cooling to rt, the mixture was diluted with 1N NaOH (50mL), extracted with EtOAc (2 x 50mL), the combined extracts washed with brine (50mL), dried ($MgSO_4$), filtered, concentrated *in vacuo*, and purified by flash chromatography on silica gel (0–25% EtOAc/hexanes) to give 3-benzoyl-2,5-dimethyl-1-(4ethoxyphenyl)pyrrole as a tan solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.84 – 7.82 (m, 2H), 7.52 – 7.43 (m, 3H), 7.14 – 7.12 (m, 2H),

7.01 – 6.98 (m, 2H), 6.18 (s, 1H), 4.10 (q, 2H), 2.33 (s, 3H), 1.98 (s, 3H), 1.47 (t, 3H). MS (ESI) 320 $(M + H)^+$.

To a solution of 3-benzoyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (201mg, 0.63mmol) and toluene (5mL) at 0°C was added dropwise $SnCl_4$ (0.76mL, 0.76mmol, 1.0M solution in CH_2Cl_2) and acetyl chloride (0.06mL, 0.76mmol). The mixture was warmed to rt overnight, quenched with 1N NaOH (10mL), extracted with EtOAc (2 x 20mL), the combined extracts washed with brine (50mL), dried ($MgSO_4$), filtered, concentrated *in vacuo*, and purified by flash chromatography on silica gel (0–33% EtOAc/hexanes). The resulting residue was dissolved in EtOH (5mL) and hydrazine (0.1mL). The solution was stirred at rt overnight and concentrated *in vacuo* to give 6-(4-ethoxyphenyl)-1-phenyl-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a tan solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.62 – 7.59 (m, 2H), 7.47 – 7.44 (m, 3H), 7.12 – 7.09 (m, 2H), 7.05 – 7.02 (m, 2H), 4.11 (q, 2H), 2.89 (s, 3H), 2.49 (s, 3H), 1.87 (s, 3H), 1.47 (t, 3H). MS (ESI) 358 $(M + H)^+$.

EXAMPLE 5

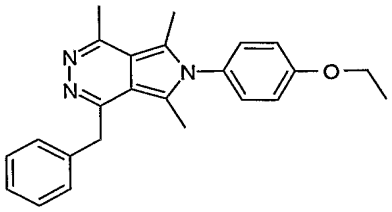
6-(4-ethoxyphenyl)-1-(3-methoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (200mg, 0.78mmol) and *m*-anisoyl chloride (0.13mL, 0.94mmol) reacted to give 6-(4-ethoxyphenyl)-1-(3-methoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a light yellow solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.38 – 7.33 (m, 1H), 7.18 – 7.14 (m, 2H), 7.13 – 7.08 (m, 2H), 7.07 – 7.02 (m, 2H), 7.01 – 6.97 (m, 1H), 4.11 (q, 2H), 3.84 (s, 3H), 2.96 (s, 3H), 2.51 (s, 3H), 1.92 (s, 3H), 1.47 (t, 3H); MS (ESI) 388 $(M + H)^+$.

EXAMPLE 6

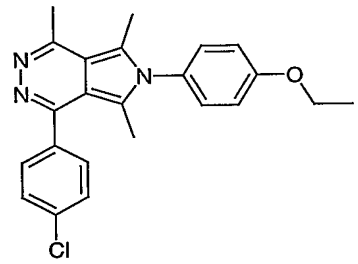
6-(4-ethoxyphenyl)-1-(3-benzyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (200mg, 0.78mmol) and phenacetyl chloride (0.16mL, 0.94mmol) reacted to give 6-(4-ethoxyphenyl)-1-(3-benzyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a light yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38 – 7.33 (m, 1H), 7.18 – 7.14 (m, 3H), 7.13 – 7.08 (m, 2H), 7.07 – 7.02 (m, 2H), 7.01 – 6.97 (m, 1H), 4.51 (s, 2H), 4.11 (q, 2H), 3.84 (s, 3H), 2.96 (s, 3H), 2.51 (s, 3H), 1.92 (s, 3H), 1.47 (t, 3H); MS (ESI) 372 $(M + H)^+$.

EXAMPLE 7

1-(4-chlorophenyl)- 6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine

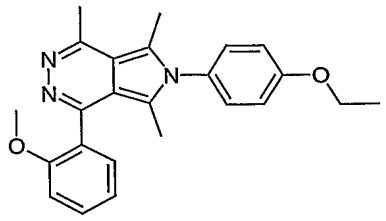


Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (200mg, 0.78mmol) and 4-chlorobenzoyl chloride (0.14mL, 0.94mmol) reacted to give 1-(4-chlorophenyl)- 6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a light yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.58 – 7.53 (m, 2H), 7.46 – 7.41 (m, 2H), 7.14 – 7.08 (m, 2H), 7.07 –

7.02 (m, 2H), 4.11 (q, 2H), 2.94 (s, 3H), 2.51 (s, 3H), 1.91 (s, 3H), 1.48 (t, 3H); MS (ESI) 392 $(M + H)^+$.

EXAMPLE 8

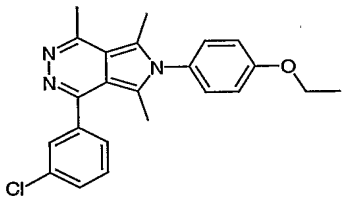
6-(4-ethoxyphenyl)-1-(2-methoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (200mg, 0.78mmol) and *o*-anisoyl chloride (0.14mL, 0.94mmol) reacted to give 6-(4-ethoxyphenyl)-1-(2-methoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a light yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.47 – 7.41 (m, 1H), 7.39 – 7.34 (m, 1H), 7.17 – 7.12 (m, 1H), 7.10 – 7.01 (m, 4H), 7.00 – 6.95 (m, 1H), 4.10 (q, 2H), 3.73 (s, 3H), 2.96 (s, 3H), 2.49 (s, 3H), 1.77 (s, 3H), 1.47 (t, 3H); MS (ESI) 388 $(M + H)^+$.

EXAMPLE 9

1-(3-chlorophenyl)- 6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine

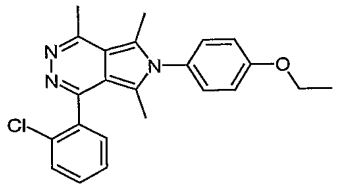


Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (200mg, 0.78mmol) and 3-chlorobenzoyl chloride (0.12mL, 0.94mmol) reacted to give 1-(3-chlorophenyl)- 6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a light yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.62 – 7.58 (m, 1H), 7.53 – 7.48 (m, 1H), 7.44 – 7.37 (m, 2H), 7.14 –

7.09 (m, 2H), 7.07 – 7.03 (m, 2H), 4.11 (q, 2H), 2.97 (s, 3H), 2.51 (s, 3H), 1.91 (s, 3H), 1.47 (t, 3H); MS (ESI) 392 $(M + H)^+$.

EXAMPLE 10

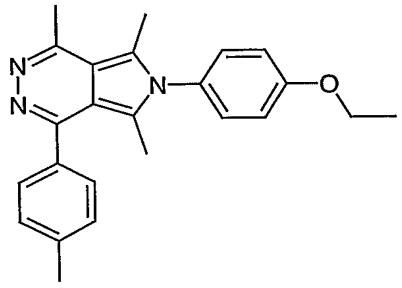
1-(2-chlorophenyl)- 6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (200mg, 0.78mmol) and 2-chlorobenzoyl chloride (0.12mL, 0.94mmol) reacted to give 1-(2-chlorophenyl)- 6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a light yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.48 – 7.43 (m, 2H), 7.40 – 7.34 (m, 2H), 7.17 – 7.12 (m, 1H), 7.08 – 6.99 (m, 3H), 4.10 (q, 2H), 2.93 (s, 3H), 2.50 (s, 3H), 1.74 (s, 3H), 1.46 (t, 3H); MS (ESI) 392 $(M + H)^+$.

EXAMPLE 11

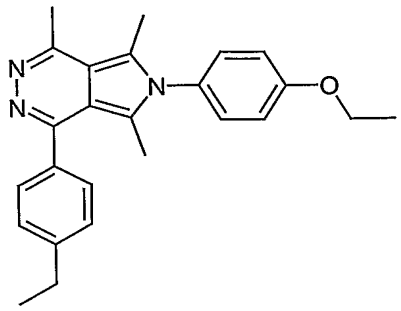
6-(4-ethoxyphenyl)-1-(4-methylphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (214mg, 0.83mmol) and *p*-toluoyl chloride (0.13mL, 1.0mmol) reacted to give 6-(4-ethoxyphenyl)-1-(4-methylphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.50 (d, 2H), 7.26 (d, 2H), 7.12 – 7.10 (m, 2H), 7.05 – 7.03 (m, 2H), 4.11 (q, 2H), 2.93 (s, 3H), 2.50 (s, 3H), 2.41 (s, 3H), 1.91 (s, 3H), 1.47 (t, 3H); MS (ESI) 372 $(M + H)^+$.

EXAMPLE 12

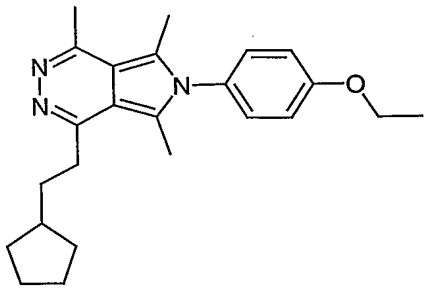
6-(4-ethoxyphenyl)-1-(4-ethylphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (214mg, 0.83mmol) and 4-ethylbenzoyl chloride (0.15mL, 1.0mmol) reacted to give 6-(4-ethoxyphenyl)-1-(4-ethylphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.54 – 7.51 (m, 2H), 7.29 – 7.25 (m, 2H), 7.12 – 7.09 (m, 2H), 7.06 – 7.03 (m, 2H), 4.11 (q, 2H), 2.93 (s, 3H), 2.71 (q, 2H), 2.50 (s, 3H), 1.91 (s, 3H), 1.47 (t, 3H), 1.26 (t, 3H); MS (ESI) 386 $(M + H)^+$.

EXAMPLE 13

1-(1-cyclopentylethyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine

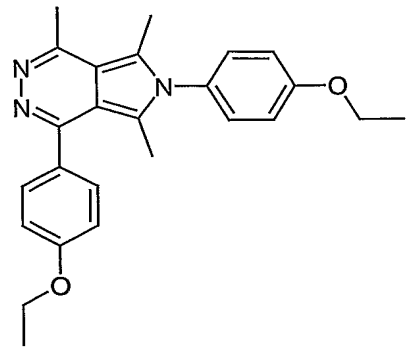


Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (257mg, 1.0mmol) and 3-cyclopentylpropionyl chloride (0.18mL, 1.2mmol) reacted to give 1-(1-cyclopentylethyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as

a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.13 – 7.09 (m, 2H), 7.07 – 7.03 (m, 2H), 4.11 (q, 2H), 3.09 (dd, 2H), 2.77 (s, 3H), 2.42 (s, 3H), 2.40 (s, 3H), 1.98 – 1.89 (m, 1H), 1.87 – 1.77 (m, 4H), 1.63 – 1.56 (m, 2H), 1.55 – 1.47 (m, 2H), 1.48 (t, 3H), 1.20 – 1.15 (m, 2H); MS (ESI) 378 $(M + H)^+$.

EXAMPLE 14

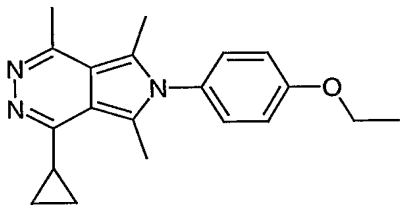
1-(4-ethoxyphenyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (214mg, 0.83mmol) and 4-ethoxybenzoyl chloride (185mg, 1.0mmol) reacted to give 1-(4-ethoxyphenyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.55 (d, 2H), 7.12 – 7.09 (m, 2H), 7.05 – 7.03 (m, 2H), 6.97 (d, 2H), 4.14 – 4.06 (m, 4H), 2.93 (s, 3H), 2.50 (s, 3H), 1.94 (s, 3H), 1.47 (t, 3H), 1.43 (t,.3H); MS (ESI) 402 $(M + H)^+$.

EXAMPLE 15

1-(cyclopropyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine

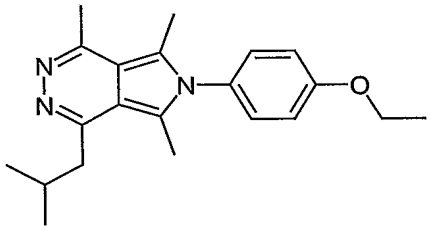


Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (257mg, 1.0mmol) and cyclopropanecarbonyl

chloride (0.11mL, 1.2mmol) reacted to give 1-(cyclopropyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.14 – 7.10 (m, 2H), 7.07 – 7.03 (m, 2H), 4.12 (q, 2H), 2.76 (s, 3H), 2.52 (s, 3H), 2.42 (s, 3H), 2.38 (quintet, 1H), 1.49 (t, 3H), 1.34 – 1.32 (m, 2H), 0.99 – 0.96 (m, 2H); MS (ESI) 322 $(M + H)^+$.

EXAMPLE 16

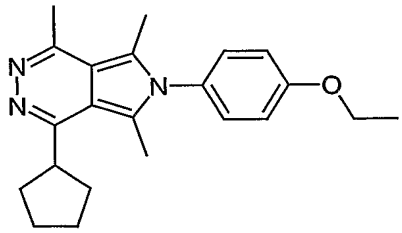
6-(4-ethoxyphenyl)-1-(2-methylpropyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (257mg, 1.0mmol) and isovaleryl chloride (0.15mL, 1.2mmol) reacted to give 6-(4-ethoxyphenyl)-1-(2-methylpropyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.12 – 7.09 (m, 2H), 7.06 – 7.03 (m, 2H), 4.12 (q, 2H), 2.94 (d, 2H), 2.78 (s, 3H), 2.42 (s, 3H), 2.38 (s, 3H), 2.18 – 2.10 (m, 1H), 1.48 (t, 3H), 1.01 (d, 6H); MS (ESI) 338 $(M + H)^+$.

EXAMPLE 17

1-(cyclopentyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine

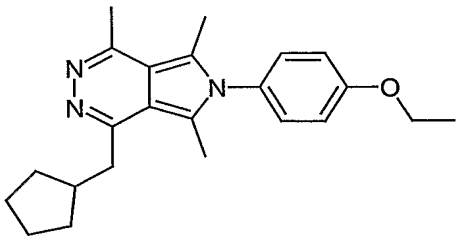


Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (257mg, 1.0mmol) and cyclopentanecarbonyl chloride (0.15mL, 1.2mmol) reacted to give 1-(cyclopentyl)-6-(4-ethoxyphenyl)-4,5,7-

trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.12 – 7.09 (m, 2H), 7.06 – 7.02 (m, 2H), 4.12 (q, 2H), 3.67 (quintet, 1H), 2.77 (s, 3H), 2.42 (s, 6H), 2.26 – 2.19 (m, 2H), 2.02 – 1.93 (m, 2H), 1.92 – 1.84 (m, 2H) 1.70 – 1.63 (m, 2H), 1.48 (t, 3H); MS (ESI) 350 $(M + H)^+$.

EXAMPLE 18

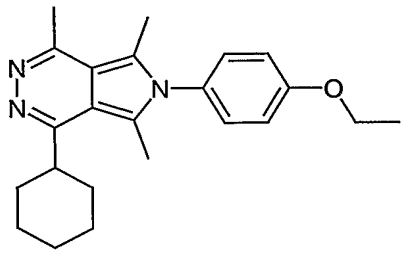
1-(cyclopentylmethyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (257mg, 1.0mmol) and cyclopentylacetyl chloride (176mg, 1.2mmol) reacted to give 1-(cyclopentylmethyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.13 – 7.09 (m, 2H), 7.06 – 7.02 (m, 2H), 4.12 (q, 2H), 3.08 (d, 2H), 2.78 (s, 3H), 2.42 (s, 3H), 2.40 (s, 3H), 2.41 – 2.32 (m, 1H), 1.79 – 1.72 (m, 2H), 1.70 – 1.62 (m, 2H) 1.55 – 1.46 (m, 2H), 1.48 (t, 3H), 1.44 – 1.37 (m, 2H); MS (ESI) 364 $(M + H)^+$.

EXAMPLE 19

1-(cyclohexyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine

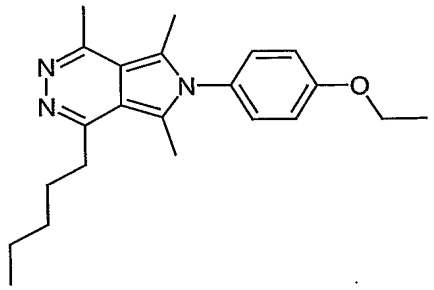


Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (257mg, 1.0mmol) and cyclohexanecarbonyl

chloride (0.16mL, 1.2mmol) reacted to give 1-(cyclohexyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.12 – 7.08 (m, 2H), 7.06 – 7.02 (m, 2H), 4.12 (q, 2H), 3.14 (tt, 1H), 2.77 (s, 3H), 2.41 (s, 3H), 2.39 (s, 3H), 2.04 – 1.98 (m, 2H), 1.95 – 1.82 (m, 4H), 1.78 – 1.72 (m, 1H) 1.48 (t, 3H), 1.44 – 1.34 (m, 3H); MS (ESI) 364 $(M + H)^+$.

EXAMPLE 20

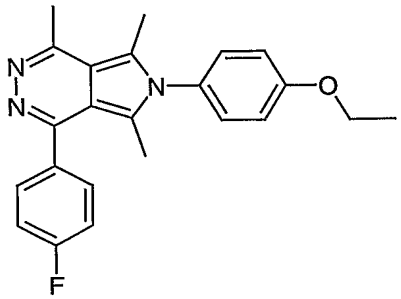
6-(4-ethoxyphenyl)-1-pentyl-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (257mg, 1.0mmol) and hexanoyl chloride (0.17mL, 1.2mmol) reacted to give 6-(4-ethoxyphenyl)-1-penyl-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.13 – 7.09 (m, 2H), 7.06 – 7.03 (m, 2H), 4.12 (q, 2H), 3.06 (dd, 2H), 2.77 (s, 3H), 2.42 (s, 3H), 2.39 (s, 3H), 1.81 – 1.75 (m, 2H), 1.50 – 1.44 (m, 2H), 1.48 (t, 3H), 1.42 – 1.34 (m, 2H), 0.89 (t, 3H); MS (ESI) 352 $(M + H)^+$.

EXAMPLE 21

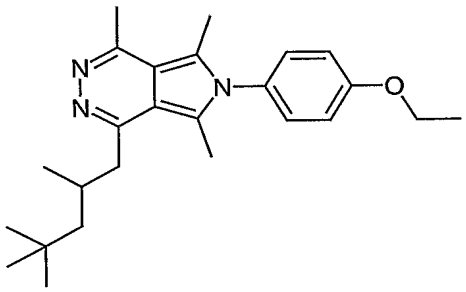
6-(4-ethoxyphenyl)-1-(4-fluorophenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (214mg, 0.83mmol) and 4-fluorobenzoyl chloride (0.12mL, 1.0mmol) reacted to give 6-(4-ethoxyphenyl)-1-(4-fluorophenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a yellowish solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.62 – 7.58 (m, 2H), 7.18 – 7.08 (m, 4H), 7.07 – 7.03 (m, 2H), 4.11 (q, 2H), 2.95 (s, 3H), 2.51 (s, 3H), 1.91 (s, 3H), 1.48 (t, 3H); MS (ESI) 376 $(M + H)^+$.

EXAMPLE 22

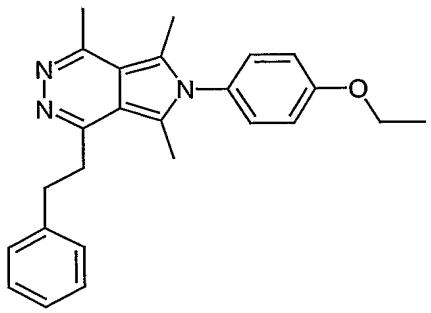
6-(4-ethoxyphenyl)-1-(2,2,4-trimethylpentyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (257mg, 1.0mmol) and 3,5,5-trimethylhexanoyl chloride (0.23mL, 1.2mmol) reacted to give 6-(4-ethoxyphenyl)-1-(2,2,4-trimethylpentyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.14 – 7.08 (m, 2H), 7.06 – 7.03 (m, 2H), 4.12 (q, 2H), 2.99 (dd, 1H), 2.92 (dd, 1H), 2.78 (s, 3H), 2.42 (s, 3H), 2.40 (s, 3H), 2.15 (quintet, 1H), 1.53 (dd, 1H), 1.49 (t, 3H), 1.21 (dd, 1H), 1.02 (d, 3H), 0.82 (s, 9H); MS (ESI) 394 $(M + H)^+$.

EXAMPLE 23

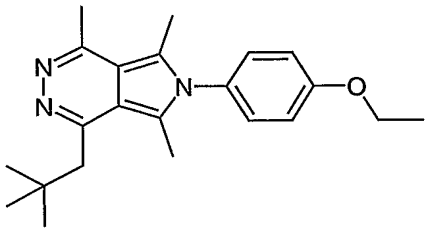
6-(4-ethoxyphenyl)-1-(1-phenylethyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (257mg, 1.0mmol) and hydrocinnamoyl chloride (0.18mL, 1.2mmol) reacted to give 6-(4-ethoxyphenyl)-1-(1-phenylethyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.31 – 7.26 (m, 4H), 7.22 – 7.18 (m, 1H), 7.12 – 7.09 (m, 2H), 7.06 – 7.04 (m, 2H), 4.12 (q, 2H), 3.38 (dd, 2H), 3.15 (dd, 2H), 2.79 (s, 3H), 2.43 (s, 3H), 2.41 (s, 3H), 1.48 (t, 3H); MS (ESI) 386 $(M + H)^+$.

EXAMPLE 24

1-(2,2-dimethylpropyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine

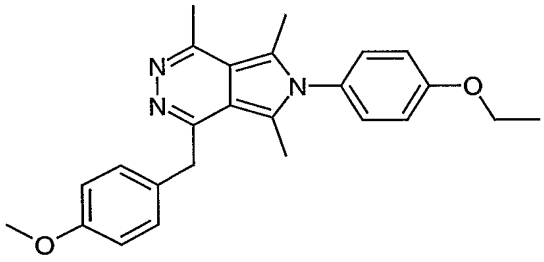


Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (257mg, 1.0mmol) and *tert*-butylacetyl chloride (0.17mL, 1.2mmol) reacted to give 1-(2,2-dimethylpropyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a white solid: ^{1}H NMR

($CDCl_3$, 500 MHz) δ 7.12 – 7.08 (m, 2H), 7.06 – 7.02 (m, 2H), 4.12 (q, 2H), 3.03 (s, 2H), 2.79 (s, 3H), 2.43 (s, 3H), 2.42 (s, 3H), 1.48 (t, 3H), 1.06 (s, 9H); MS (ESI) 352 $(M + H)^+$.

EXAMPLE 25

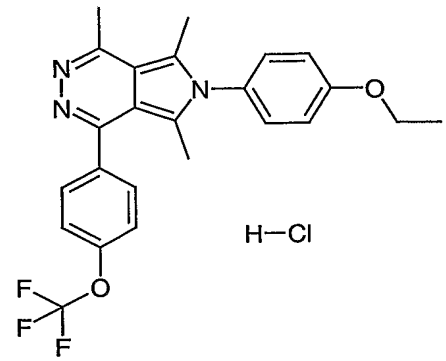
6-(4-ethoxyphenyl)-1-(4-methoxyphenylmethyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (257mg, 1.0mmol) and 4-methoxyphenylacetyl chloride (0.19mL, 1.2mmol) reacted to give 6-(4-ethoxyphenyl)-1-(4-methoxyphenylmethyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a white solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.16 (d, 2H), 7.05 – 6.98 (m, 4H), 6.76 (d, 2H), 4.39 (s, 2H), 4.09 (q, 2H), 3.74 (s, 3H), 2.81 (s, 3H), 2.41 (s, 3H), 2.19 (s, 3H), 1.46 (t, 3H); MS (ESI) 402 $(M + H)^+$.

EXAMPLE 26

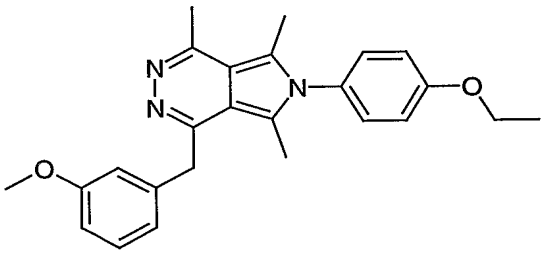
6-(4-ethoxyphenyl)-1-(4-(trifluoromethoxy)phenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (214mg, 0.83mmol) and 4-(trifluoromethoxy)benzoyl chloride (0.16mL, 1.0mmol) reacted to give the product which was taken up in hot ether, precipitated with HCl in ether, and filtered to give 6-(4-ethoxyphenyl)-1-(4-(trifluoromethoxy)phenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a yellow solid: ^{1}H NMR (d_6-DMSO, 500 MHz) δ 7.86 (d, 2H), 7.62 (d, 2H), 7.38 (d, 2H), 7.21 (d, 2H), 4.14 (q, 2H), 3.14 (s, 3H), 2.60 (s, 3H), 1.94 (s, 3H), 1.38 (t, 3H); MS (ESI) 442 $(M + H)^+$.

EXAMPLE 27

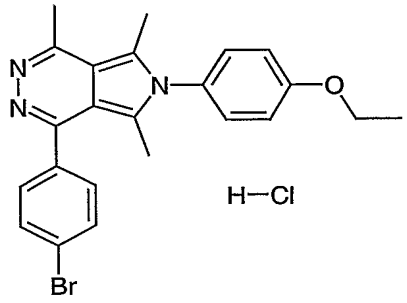
6-(4-ethoxyphenyl)-1-(3-methoxyphenylmethyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (257mg, 1.0mmol) and 3-methoxyphenylacetyl chloride (0.19mL, 1.2mmol) reacted to give 6-(4-ethoxyphenyl)-1-(3-methoxyphenylmethyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.15 (dd, 1H), 7.06 – 7.03 (m, 2H), 7.02 – 6.98 (m, 2H), 6.83 (d, 1H), 6.80 (s, 1H), 6.71 (d, 1H), 4.43 (s, 2H), 4.09 (q, 2H), 3.72 (s, 3H), 2.81 (s, 3H), 2.42 (s, 3H), 2.20 (s, 3H), 1.46 (t, 3H); MS (ESI) 402 $(M + H)^+$.

EXAMPLE 28

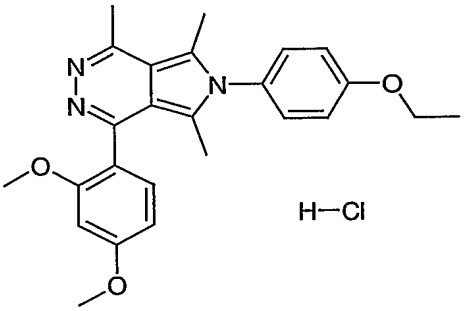
1-(4-bromophenyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (214mg, 0.83mmol) and *p*-bromobenzoyl chloride (220mg, 1.0mmol) reacted to give the product which was taken up in hot ether, precipitated with HCl in ether, and filtered to give 1-(4-bromophenyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride as a yellow solid: ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.83 (d, 2H), 7.66 (d, 2H), 7.37 (d, 2H), 7.20 (d, 2H), 4.14 (q, 2H), 3.12 (s, 3H), 2.59 (s, 3H), 1.94 (s, 3H), 1.38 (t, 3H); MS (ESI) 437 $(M + H)^+$.

EXAMPLE 29

1-(2,4-dimethoxyphenyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride

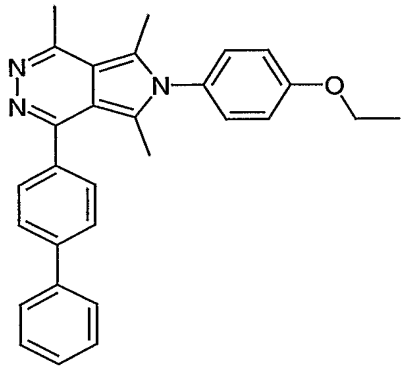


Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (214mg, 0.83mmol) and 2,4-dimethoxybenzoyl chloride (201mg, 1.0mmol) reacted to give the product which was

taken up in hot ether, precipitated with HCl in ether, and filtered to give 1-(2,4-dimethoxyphenyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride as a yellow solid: ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.41 – 7.30 (m, 3H), 7.18 (d, 2H), 6.80 – 6.73 (m, 2H), 4.14 (q, 2H), 3.87 (s, 3H), 3.76 (s, 3H), 3.03 (br s, 3H), 2.54 (s, 3H), 1.87 (s, 3H), 1.38 (t, 3H); MS (ESI) 418 $(M + H)^+$.

EXAMPLE 30

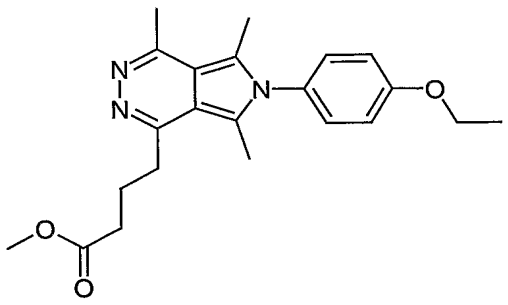
1-(4-biphenyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (214mg, 0.83mmol) and 4-biphenylcarbonyl chloride (217mg, 1.0mmol) reacted to give 1-(4-biphenyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.73 – 7.64 (m, 4H), 7.60 (d, 2H), 7.45 (t, 2H), 7.35 (t, 1H), 7.11 (d, 2H), 7.03 (d, 2H), 4.11 (q, 2H), 2.87 (s, 3H), 2.49 (s, 3H), 1.95 (s, 3H), 1.47 (t, 3H); MS (ESI) 434 $(M + H)^+$.

EXAMPLE 31

4-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-yl]-butyric acid methyl ester

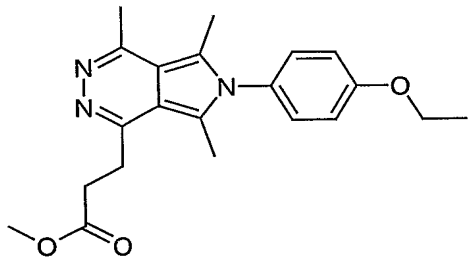


Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (771mg, 3.0mmol) and methyl 5-chloro-5-oxovalerate (0.63mL, 4.5mmol) reacted to give 5-[4-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)-1*H*-pyrrol-3-yl]-5-oxo-pentanoic acid methyl ester as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.05 (d, 2H), 6.98 (d, 2H), 4.08 (q, 2H), 3.65 (s, 3H), 2.75 (t, 2H), 2.41 (s, 3H), 2.40 (t, 2H), 2.11 (s, 3H), 2.01 (s, 3H), 2.00 (quintet, 2H), 1.45 (t, 3H); MS (ESI) 386 $(M + H)^+$.

To a solution of 5-[4-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)-1*H*-pyrrol-3-yl]-5-oxo-pentanoic acid methyl ester (250mg, 0.65mmol) in ethanol (1mL) was added a 1.0M solution of hydrazine in ethanol (0.72mL, 0.72mmol). The solution was stirred overnight at rt and concentrated *in vacuo* to give 4-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-yl]-butyric acid methyl ester as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.11 – 7.08 (m, 2H), 7.05 – 7.03 (m, 2H), 4.11 (q, 2H), 3.63 (s, 3H), 3.12 (t, 2H), 2.77 (s, 3H), 2.51 (t, 2H), 2.41 (s, 3H), 2.40 (s, 3H), 2.14 (quintet, 2H), 1.47 (t, 3H); MS (ESI) 382 $(M + H)^+$.

EXAMPLE 32

4-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-yl]-propionic acid methyl ester

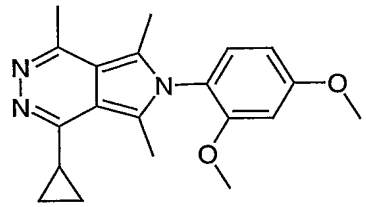


Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)pyrrole (771mg, 3.0mmol) and methyl 4-chloro-4-oxobutyrate (0.56mL, 4.5mmol) reacted to give 4-[4-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)-1*H*-pyrrol-3-yl]-4-oxo-butyric acid methyl ester as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.06 (d, 2H), 6.98 (d, 2H), 4.08 (q, 2H), 3.67 (s, 3H), 3.03 (t, 2H), 2.74 (t, 2H), 2.41 (s, 3H), 2.11 (s, 3H), 2.06 (s, 3H), 1.45 (t, 3H); MS (ESI) 372 $(M + H)^+$.

To a solution of 4-[4-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)-1*H*-pyrrol-3-yl]-4-oxo-butyric acid methyl ester (250mg, 0.67mmol) in ethanol (1mL) was added a 1.0M solution of hydrazine in ethanol (0.74mL, 0.74mmol). The solution was stirred overnight at rt and concentrated *in vacuo* to give 4-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-yl]-propionic acid methyl ester as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.11 – 7.08 (m, 2H), 7.06 – 7.03 (m, 2H), 4.12 (q, 2H), 3.70 (s, 3H), 3.43 (t, 2H), 3.00 (t, 2H), 2.79 (s, 3H), 2.44 (s, 3H), 2.42 (s, 3H), 1.48 (t, 3H); MS (ESI) 368 $(M + H)^+$.

EXAMPLE 33

1-(cyclopropyl)-6-(2,4-dimethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



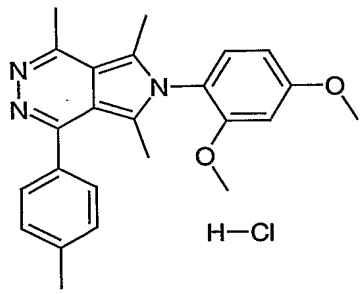
Utilizing the general procedure outlined in **EXAMPLE 1**, acetonyl acetone (5.88mL, 50mmol) and 2,4-dimethoxyaniline (7.12mL, 50mmol) reacted to give 1-(2,4-dimethoxyphenyl)-2,5-dimethylpyrrole as a tan solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.08 (dd, 1H), 6.59 (d, 1H), 6.55 (dd, 1H), 5.90 (s, 2H), 3.91 (s, 3H), 3.80 (s, 3H), 1.97 (s, 6H); MS (ESI) 232 $(M + H)^+$.

Utilizing the general procedure outlined in **EXAMPLE 1**, 1-(2,4-dimethoxyphenyl)-2,5-dimethylpyrrole (2.31g, 10mmol), acetic anhydride (5mL), and hydriodic acid (0.13mL, 1.7mmol) reacted to give 3-acetyl-1-(2,4-dimethoxyphenyl)-2,5-dimethylpyrrole as a tan solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.02 (dd, 1H), 6.59 (d, 1H), 6.55 (dd, 1H), 6.32 (s, 1H), 3.90 (s, 3H), 3.76 (s, 3H), 2.42 (s, 3H), 2.25 (s, 3H), 1.93 (s, 3H); MS (ESI) 274 $(M + H)^+$.

To a solution of 3-acetyl-1-(2,4-dimethoxyphenyl)-2,5-dimethylpyrrole (273mg, 1.0mmol) in toluene (5mL) at -78°C was added 3-cyclopropanecarbonyl chloride (0.11mL, 1.2mmol) followed by dropwise addition of a 1.0M solution of tin(IV) chloride inCH2Cl2(1.2mL, 1.2mmol). The reaction was allowed to warm to room temp overnight. The solution was diluted with 0.25M NaOH, extracted with EtOAc, the organic layer washed with brine, dried over $MgSO_4$, filtered, concentrated *in vacuo*, and purified by flash chromatography (10-25% EtOAc/hexanes) to give the dione (MS (ESI) 342 $(M + H)^+$). The dione was taken up in ethanol (5mL) and excess hydrazine (0.1mL) was added. The solution was stirred at 40°C overnight, poured into water, and filtered to give 1-(cyclopropyl)-6-(2,4-dimethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.03 (dd, 1H), 6.66 – 6.56 (m, 2H), 3.90 (s, 3H), 3.75 (s, 3H), 2.75 (s, 3H), 2.47 (s, 3H), 2.39 (quintet, 1H), 2.38 (s, 3H), 1.35 – 1.28 (m, 2H), 0.97 (dd, 2H); MS (ESI) 338 $(M + H)^+$.

EXAMPLE 34

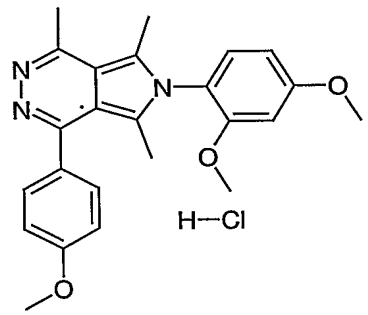
6-(2,4-dimethoxyphenyl)-1-(4-methylphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride



Utilizing the general procedure outlined in **EXAMPLE 33**, 3-acetyl-1-(2,4-dimethoxyphenyl)-2,5-dimethylpyrrole (273mg, 1.0mmol) and *p*-toluoyl chloride (0.27mL, 2.0mmol) reacted to give the product as a clear oil which was taken up in ether, precipitated with HCl in ether, and filtered to give 6-(2,4-dimethoxyphenyl)-1-(4-methylphenyl)- 4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride as a yellow solid: ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.58 – 7.51 (m, 2H), 7.45 – 7.37 (m, 2H), 7.33 (dd, 1H), 6.92 (d, 1H), 6.79 (dd, 1H), 3.90 (s, 3H), 3.77 (s, 3H), 3.08 (br s, 3H), 2.50 (br s, 3H), 2.44 (s, 3H), 1.90 (s, 3H); MS (ESI) 388 $(M + H)^+$.

EXAMPLE 35

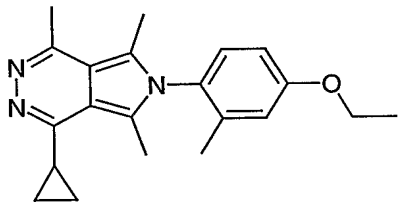
6-(2,4-dimethoxyphenyl)-1-(4-methoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride



Utilizing the general procedure outlined in **EXAMPLE 33**, 3-acetyl-1-(2,4-dimethoxyphenyl)-2,5-dimethylpyrrole (273mg, 1.0mmol) and *p*-anisoyl chloride (0.28mL, 2.0mmol) reacted to give the product as a clear oil which was taken up in ether, precipitated with HCl in ether, and filtered to give 6-(2,4-dimethoxyphenyl)-1-(4-methoxyphenyl)- 4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride as a yellow solid: ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.58 – 7.51 (m, 2H), 7.45 – 7.37 (m, 2H), 7.33 (dd, 1H), 6.92 (d, 1H), 6.79 (dd, 1H), 3.90 (s, 3H), 3.87 (s 3H), 3.77 (s, 3H), 3.08 (br s, 3H), 2.50 (s, 3H), 2.00 (s, 3H); MS (ESI) 404 $(M + H)^+$.

EXAMPLE 36

1-(cyclopropyl)-6-(4-ethoxy-2-methylphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 1**, acetonyl acetone (5.88mL, 50mmol) and *o*-cresol (6.12, 50mmol) reacted to give 1-(4-hydroxy-2-methylphenyl)-2,5-dimethylpyrrole as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.05 (d, 1H), 6.80 (d, 1H), 6.75 (dd, 1H), 5.96 (s, 2H), 5.10 (br s, 1H), 1.96 (s, 6H), 1.92 (s, 3H); MS (ESI) 202 $(M + H)^+$.

To a solution of 1-(4-hydroxy-2-methylphenyl)-2,5-dimethylpyrrole (~50mmol) in acetonitrile (300mL) was added potassium carbonate (55mmol) and an excess of bromoethane (>100mmol). The reaction mixture was stirred at 50°C overnight, cooled to room temperature, and partitioned between EtOAc and water. The organic layer was washed with brine, dried over $MgSO_4$, filtered, concentrated *in vacuo*, and purified by column chromatography (15% EtOAc/hexanes) to give 2,5-dimethyl-1-(4-ethoxy-2-methylphenyl)pyrrole as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.07 (d, 1H), 6.84 (d, 1H), 6.79 (dd, 1H), 5.90 (s, 2H), 4.07 (q, 2H), 1.92 (s, 6H), 1.90 (s, 3H), 1.45 (t, 3H); MS (ESI) 230 $(M + H)^+$.

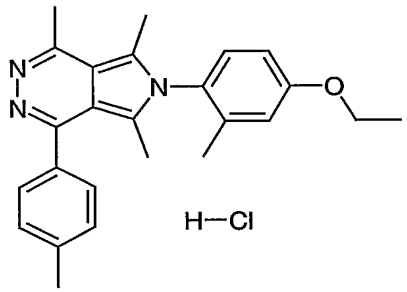
Utilizing the general procedure outlined in **EXAMPLE 1**, 2,5-dimethyl-1-(4-ethoxy-2-methylphenyl)pyrrole (2.29g, 10mmol), acetic anhydride

(5mL), and hydriodic acid (0.13mL, 1.7mmol) reacted to give 3-acetyl-2,5-dimethyl-1-(4-ethoxy-2-methylphenyl)pyrrole as a tan solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.99 (d, 1H), 6.85 (d, 1H), 6.79 (dd, 1H), 6.32 (s, 1H), 4.06 (q, 2H), 2.42 (s, 3H), 2.22 (s, 3H), 1.89 (s, 3H), 1.88 (s, 3H), 1.44 (t, 3H); MS (ESI) 272 $(M + H)^+$.

Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxy-2-methylphenyl)pyrrole (271mg, 1.0mmol) and 3-cyclopropanecarbonyl chloride (0.11mL, 1.2mmol) reacted to give 1-(cyclopropyl)-6-(4-ethoxy-2-methylphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.03 (d, 1H), 6.92 (d, 1H), 6.88 (dd, 2H), 4.10 (q, 2H), 2.76 (s, 3H), 2.45 (s, 3H), 2.38 (quintet, 1H), 2.35 (s, 3H), 1.83 (s, 3H), 1.47 (t, 3H), 1.39 – 1.31 (m, 2H), 0.98 (dd, 2H); MS (ESI) 336 $(M + H)^+$.

EXAMPLE 37

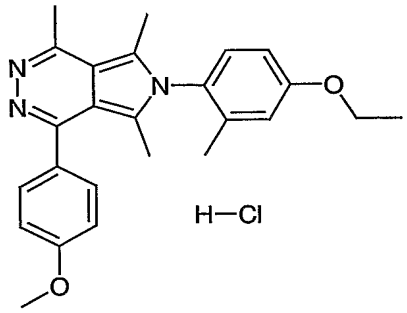
6-(4-ethoxy-2-methylphenyl)-1-(4-methylphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride



Utilizing the general procedure outlined in **EXAMPLE 36**, 3-acetyl-2,5-dimethyl-1-(4-ethoxy-2-methylphenyl)pyrrole (271mg, 1.0mmol) and *p*-toluoyl chloride (0.27mL, 2.0mmol) reacted to give the product as a clear oil which was taken up in ether, precipitated with HCl in ether, and filtered to give 6-(4-ethoxy-2-methylphenyl)-1-(4-methylphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride as a yellow solid: ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.63 – 7.59 (m, 2H), 7.47 – 7.39 (m, 2H), 7.24 (d, 1H), 7.13 (d, 1H), 7.03 (dd, 1H), 4.12 (q, 2H), 3.09 (br s, 3H), 2.51 (br s, 3H), 2.44 (s, 3H), 1.89 (s, 3H), 1.83 (s, 3H), 1.37 (t, 3H); MS (ESI) 386 $(M + H)^+$.

EXAMPLE 38

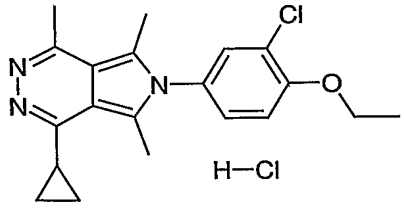
6-(4-ethoxy-2-methylphenyl)-1-(4-methoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride



Utilizing the general procedure outlined in **EXAMPLE 36**, 3-acetyl-2,5-dimethyl-1-(4-ethoxy-2-methylphenyl)pyrrole (271mg, 1.0mmol) and *p*-anisoyl chloride (0.28mL, 2.0mmol) reacted to give the product as a clear oil which was taken up in ether, precipitated with HCl in ether, and filtered to give 6-(4-ethoxy-2-methylphenyl)-1-(4-methoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride as a yellow solid: ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.63 – 7.59 (m, 2H), 7.47 – 7.39 (m, 2H), 7.24 (d, 1H), 7.13 (d, 1H), 7.03 (dd, 1H), 4.12 (q, 2H), 3.87 (s, 3H), 3.09 (br s, 3H), 2.51 (br s, 3H), 2.44 (s, 3H), 1.89 (s, 3H), 1.37 (t, 3H); MS (ESI) 404 $(M + H)^+$.

EXAMPLE 39

6-(3-chloro-4-ethoxyphenyl)-1-(cyclopropyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride



Utilizing the general procedure outlined in **EXAMPLE 1**, acetonyl acetone (0.83mL, 7.0mmol) and 4-amino-2-chlorophenol (1.0g, 7.0mmol) reacted to give 1-(3-chloro-4-hydroxyphenyl)-2,5-dimethylpyrrole as a brown solid: ^{1}H NMR

($CDCl_3$, 500 MHz) δ 7.22 (d, 1H), 7.10 (d, 1H), 7.05 (dd, 1H), 5.88 (s, 2H), 5.66 (br s, 1H), 2.03 (s, 6H); MS (ESI) 222 $(M + H)^+$.

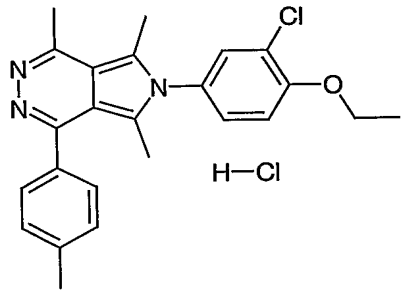
Using the general procedure outlined in **EXAMPLE 1**, 1-(3-chloro-4-hydroxyphenyl)-2,5-dimethylpyrrole (1.11g, 5mmol) and an excess of bromoethane (1.0mL) reacted to give 1-(3-chloro-4-ethoxyphenyl)-2,5-dimethylpyrrole as a tan solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.27 (d, 1H), 7.08 (dd, 1H), 6.99 (dd, 1H), 5.89 (s, 2H), 4.18 (q, 2H), 2.04 (s, 6H), 1.53 (t, 3H); MS (ESI) 250 $(M + H)^+$.

Utilizing the general procedure outlined in **EXAMPLE 1**, 1-(3-chloro-4-ethoxyphenyl)-2,5-dimethylpyrrole (1.21g, 4.8mmol), acetic anhydride (5mL), and hydriodic acid (0.07mL, 0.83mmol) reacted to give 3-acetyl-1-(3-chloro-4-ethoxyphenyl)-2,5-dimethylpyrrole as a tan solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.21 (d, 1H), 7.04 – 6.98 (m, 2H), 6.29 (s, 1H), 4.17 (q, 2H), 2.41 (s, 3H), 2.30 (s, 3H), 1.98 (s, 3H), 1.52 (t, 3H); MS (ESI) 292 $(M + H)^+$.

Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-1-(3-chloro-4-ethoxyphenyl)-2,5-dimethylpyrrole (291mg, 1.0mmol) and 3-cyclopropanecarbonyl chloride (0.18mL, 2.0mmol) reacted to give the product as a clear oil which was taken up in ether, precipitated with HCl in ether, and filtered to give 6-(3-chloro-4-ethoxyphenyl)-1-(cyclopropyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride as a yellow solid: ^1H NMR (DMSO-d_6, 500 MHz) δ 7.70 (s, 1H), 7.46 – 7.41 (m, 2H), 4.26 (q, 2H), 2.99 (br s, 3H), 2.67 – 2.61 (m, 1H), 2.58 (s, 3H), 2.52 (s, 3H), 1.43 (t, 3H), 1.28 – 1.12 (m, 4H); MS (ESI) 356 $(M + H)^+$.

EXAMPLE 40

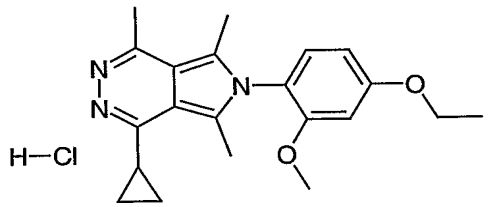
6-(3-chloro-4-ethoxyphenyl)-1-(4-methylphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride



Utilizing the general procedure outlined in **EXAMPLE 39**, 3-acetyl-1-(3-chloro-4-ethoxyphenyl)-2,5-dimethylpyrrole (291mg, 1.0mmol) and *p*-toluoyl chloride (0.27mL, 2.0mmol) reacted to give the product as a clear oil which was taken up in ether, precipitated with HCl in ether, and filtered to give 6-(3-chloro-4-ethoxyphenyl)-1-(4-methylphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride as a green solid: ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.71 (d, 1H), 7.63 – 7.57 (m, 2H), 7.45 – 7.39 (m, 4H), 4.25 (q, 2H), 3.08 (br s, 3H), 2.44 (s, 3H), 1.96 (s, 3H), 1.41 (t, 3H); MS (ESI) 406 $(M + H)^+$.

EXAMPLE 41

1-(cyclopropyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride



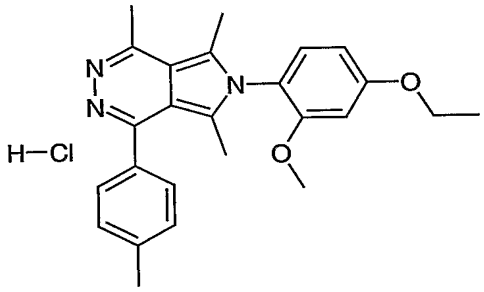
To a solution of 3-acetyl-1-(2,4-dimethoxyphenyl)-2,5-dimethylpyrrole (2.73g, 10mmol) (**EXAMPLE 33**) inCH_2Cl_2at rt (75mL) was added a 1.0M solution of boron tribromide inCH_2Cl_2(15mL, 15mmol) and the reaction monitored by LC. After complete consumption of the starting material, the reaction was carefully quenched with saturated $NaHCO_3$ and partitioned between EtOAc and water. The organic layer was washed with brine, dried over $MgSO_4$, filtered, concentrated *in vacuo*, and purified by flash chromatography to give 3-acetyl-2,5-dimethyl-1-(4-hydroxy-2-methoxyphenyl)pyrrole as a tan solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.92 (d, 1H), 6.61 (d, 1H), 6.54 (dd, 1H), 6.32 (s, 1H), 3.72 (s, 3H), 2.44 (s, 3H), 2.26 (s, 3H), 1.93 (s, 3H), 1.69 (br s, 1H); MS (ESI) 260 $(M + H)^+$.

Using the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-hydroxy-2-methoxyphenyl)pyrrole (1.37g, 5.3mmol) and an excess of bromoethane (2.0mL) reacted to give 3-acetyl-2,5-dimethyl-1-(4-ethoxy-2-methoxyphenyl)pyrrole as a tan solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.99 (d, 1H), 6.59 (d, 1H), 6.53 (dd, 1H), 6.31 (s, 1H), 4.08 (q, 2H), 3.74 (s, 3H), 2.41 (s, 3H), 2.25 (s, 3H), 1.93 (s, 3H), 1.46 (t, 3H); MS (ESI) 288 $(M + H)^+$.

Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxy-2-methoxyphenyl)pyrrole (241mg, 0.84mmol) and 3-cyclopropanecarbonyl chloride (0.10mL, 1.0mmol) reacted to give the product which was taken up in ether, precipitated with HCl in ether, and filtered to give 1-(cyclopropyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride as a yellow solid: ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.29 (d, 1H), 6.92 (d, 1H), 6.79 (dd, 2H), 4.18 (q, 2H), 3.77 (s, 3H), 3.45 (br s, 3H), 2.99 (br s, 3H), 2.64 (m, 1H), 2.46 (s, 3H), 1.40 (t, 3H), 1.20 – 1.12 (m, 4H); MS (ESI) 352 $(M + H)^+$.

EXAMPLE 42

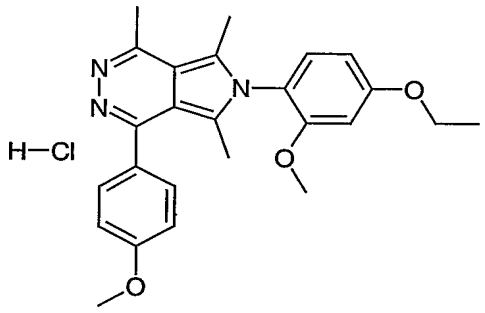
6-(4-ethoxy-2-methoxyphenyl)-1-(4-methylphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxy-2-methoxyphenyl)pyrrole (**EXAMPLE 34**) (241mg, 0.84mmol) and *p*-toluoyl chloride (0.13mL, 1.0mmol) reacted to give the product as a clear oil which was taken up in ether, precipitated with HCl in ether, and filtered to give 6-(4-ethoxy-2-methoxyphenyl)-1-(4-methylphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride as a yellow solid: ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.59 – 7.53 (m, 2H), 7.46 – 7.42 (m, 2H), 7.28 (d, 1H), 6.88 (d, 1H), 6.76 (dd, 1H), 4.15 (q, 2H), 3.75 (s, 3H), 3.56 (br s, 3H), 3.10 (br s, 3H), 2.43 (s, 3H), 1.89 (s, 3H), 1.38 (t, 3H); MS (ESI) 402 $(M + H)^+$.

EXAMPLE 43

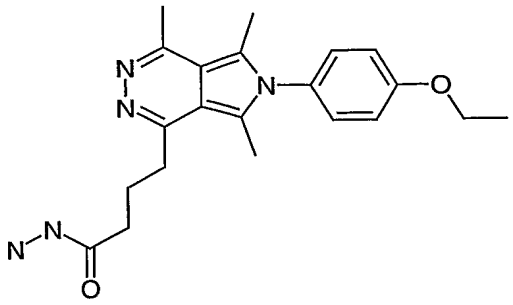
6-(4-ethoxy-2-methoxyphenyl)-1-(4-methoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride



Utilizing the general procedure outlined in **EXAMPLE 1**, 3-acetyl-2,5-dimethyl-1-(4-ethoxy-2-methoxyphenyl)pyrrole (EXAMPLE 35) (241mg, 0.84mmol) and *p*-anisoyl chloride (0.15mL, 1.0mmol) reacted to give the product as a clear oil which was taken up in ether, precipitated with HCl in ether, and filtered to give 6-(4-ethoxy-2-methoxyphenyl)-1-(4-methoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride as a yellow solid: ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.69 – 7.62 (m, 2H), 7.29 (d, 1H), 7.19 – 7.13 (m, 2H), 6.90 (d, 1H), 6.77 (dd, 1H), 4.16 (q, 2H), 3.87 (s, 3H), 3.76 (s, 3H), 3.65 (br s, 3H), 3.05 (br s, 3H), 1.93 (s, 3H), 1.38 (t, 3H); MS (ESI) 418 $(M + H)^+$.

EXAMPLE 44

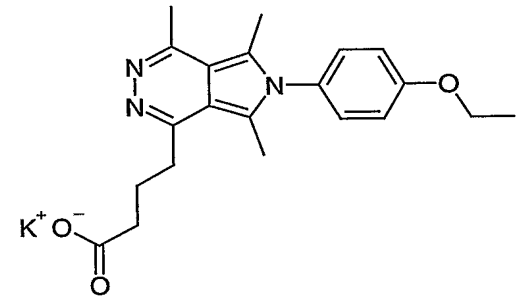
4-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-yl]-butyric acid hydrazide



To a solution of 5-[4-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)-1*H*-pyrrol-3-yl]-5-oxo-pentanoic acid methyl ester (100mg, 0.26mmol) (**EXAMPLE 31**) in ethanol (1mL) was added excess hydrazine (0.1mL). The solution was stirred overnight at 50°C and concentrated *in vacuo* to give 4-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-yl]-butyric acid hydrazide as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.04 (br s, 1H), 7.12 – 7.09 (m, 2H), 7.06 – 7.03 (m, 2H), 4.11 (q, 2H), 3.78 (br s, 2H), 3.15 (t, 2H), 2.78 (s, 3H), 2.43 (s, 3H), 2.41 (s, 3H), 2.32 (t, 2H), 2.18 – 2.12 (m, 2H), 1.48 (t, 3H); MS (ESI) 382 $(M + H)^+$.

EXAMPLE 45

4-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-yl]-butyric acid potassium salt

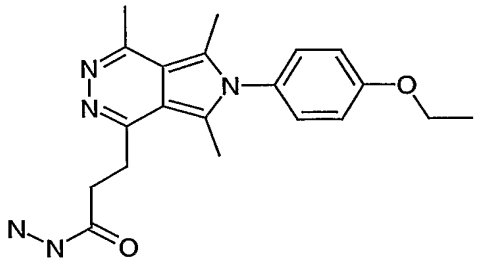


To a solution of 4-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-yl]-butyric acid methyl ester (104mg, 0.27mmol) (**EXAMPLE 31**) in THF (3mL) was added potassium trimethylsilanoate (57mg, 0.4mmol). The mixture was stirred overnight and filtered to give 4-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-yl]-butyric acid potassium salt as a tan solid: ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.27 (d, 2H), 7.12 (d, 2H), 4.12 (q, 2H), 2.90 (t, 2H), 2.64 (s,

3H), 2.37 (s, 3H), 2.36 (s, 3H), 1.91 (t, 2H), 1.80 – 1.75 (m, 2H), 1.37 (t, 3H); MS (ESI) 368 $(M + H)^+$.

EXAMPLE 46

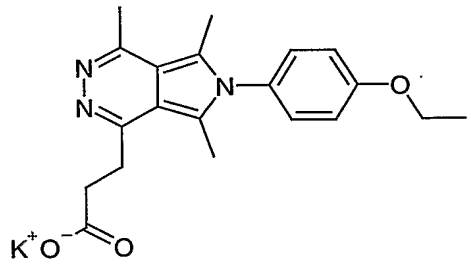
4-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-yl]-propionic acid hydrazide



Utilizing the general procedure outlined in **EXAMPLE 44**, 4-[4-acetyl-2,5-dimethyl-1-(4-ethoxyphenyl)-1*H*-pyrrol-3-yl]-4-oxo-butyric acid methyl ester (100mg, 0.27mmol) (**EXAMPLE 32**) and excess hydrazine (0.1mL) reacted to give 4-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-yl]-propionic acid hydrazide as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.62 (br s, 1H), 7.13 – 7.08 (m, 2H), 7.07 – 7.04 (m, 2H), 4.12 (q, 2H), 3.49 (t, 2H), 3.09 (br s, 2H), 2.91 (t, 2H), 2.83 (s, 3H), 2.46 (s, 3H), 2.44 (s, 3H), 1.49 (t, 3H); MS (ESI) 368 $(M + H)^+$.

EXAMPLE 47

4-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-yl]-propionic acid potassium salt

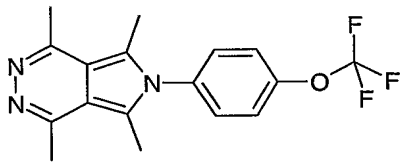


Utilizing the general procedure outlined in **EXAMPLE 45**, 4-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-yl]-propionic acid methyl ester (100mg, 0.27mmol) (**EXAMPLE 32**) and potassium trimethylsilanoate

(57mg, 0.4mmol) reacted to give 4-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-yl]-propionic acid potassium salt as a tan solid: ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.27 (d, 2H), 7.12 (d, 2H), 4.12 (q, 2H), 3.09 (dd, 2H), 2.63 (s, 3H), 2.36 (s, 3H), 2.35 (s, 3H), 2.15 (dd, 2H), 1.37 (t, 3H); MS (ESI) 354 (M + H)$^+$.

EXAMPLE 48

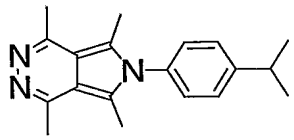
1,4,5,7-tetramethyl-6-[4-(trifluoromethoxy)phenyl]-6*H*-pyrrolo[3,4-*d*]pyridazine



A solution of 1,1,2,2-tetraacetylethane (250mg, 1.26mmol) and 4-trifluoromethoxy aniline (170μL, 1.26mmol) was refluxed in EtOH (5mL)/AcOH (1%) for 48h. Hydrazine (100μL, 3.15mmol) was added and the mixture was refluxed for 1h. The reaction mixture was poured into ice water (50mL). The resulting precipitate was filtered and dried under vacuum to afford 1,4,5,7-tetramethyl-6-[4-(trifluoromethoxy)phenyl]-6*H*-pyrrolo[3,4-*d*]pyridazine as a tan solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.42 (d, 2H), 7.25 (d, 2H), 2.81 (s, 6H), 2.41 (s, 6H); MS (ESI) 336 (M+H)$^+$.

EXAMPLE 49

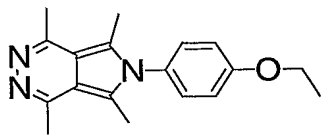
6-(4-isopropylphenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 48**, 1,1,2,2-tetraacetylethane (250mg, 1.26mmol) and 4-isopropyl aniline (172μL, 1.26mmol) reacted to give 6-(4-isopropylphenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a tan solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.40 (d, 2H), 7.07 (d, 2H), 3.01-2.97 (m, 1H) 2.83 (s, 6H), 2.41 (s, 6H) 1.28 (d, 6H); MS (ESI) 294 (M+H)$^+$.

EXAMPLE 50

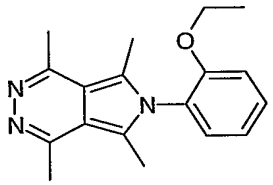
6-(4-ethoxy)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 48**, 1,1,2,2-tetraacetylethane (250mg, 1.26mmol) and *p*-phenetidine (172μL, 1.26mmol) reacted to give 6-(4-ethoxyphenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a tan solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.41-7.39 (d, 2H), 7.07-7.06 (d, 2H), 4.07 (q, 2H), 2.83 (s, 6H), 2.41 (s, 6H) 1.45 (t, 6H); MS (ESI) 294 $(M+H)^+$.

EXAMPLE 51

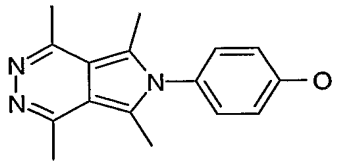
6-(2-ethoxy)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 48**, 1,1,2,2-tetraacetylethane (250mg, 1.26mmol) and *o*-phenetidine (172μL, 1.26mmol) reacted to give 6-(2-ethoxyphenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a tan solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.41-7.39 (d, 2H), 7.07-7.06 (d, 2H), 4.12 (q, 2H), 2.83 (s, 6H), 2.41 (s, 6H) 1.55 (t, 6H); MS (ESI) 294 $(M+H)^+$.

EXAMPLE 52

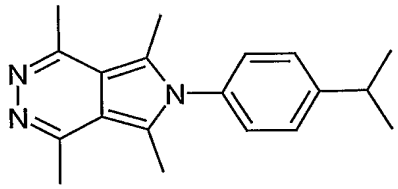
6-(4-hydroxyphenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 48**, 1,1,2,2-tetraacetylethane (250 mg, 1.26mmol) and 4-aminophenol (172μL, 1.26mmol) reacted to give 6-(4-hydroxyphenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a tan solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.41-7.39 (d, 2H), 7.07-7.06 (d, 2H), 2.83 (s, 6H), 2.41 (s, 6H); MS (ESI) 266 $(M+H)^+$.

EXAMPLE 53

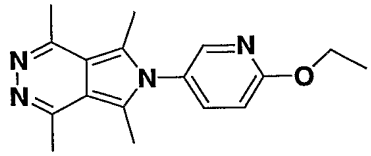
6-(4-isopropylphenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **Example 48**, 1,1,2,2-tetraacetylethane (250mg, 1.26 mmol) and 4-isopropyl aniline (172 μL, 1.26 mmol) reacted to give 6-(4-isopropylphenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a tan solid. ^{1}H NMR ($CDCl_3$, 500MHz) δ 7.41-7.39 (d, 2H), 7.07-7.06 (d, 2H), 3.01-2.97 (m, 1H) 2.83 (s, 6H), 2.41 (s, 6H) 1.28-1.27 (d, 6H). MS 294 (M+H).

EXAMPLE 54

6-(6-Ethoxy-pyridin-3-yl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



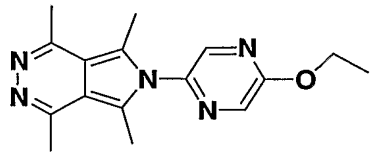
Utilizing the general procedure outlined in **Example 48,** 1,1,2,2-tetraacetylethane (200 mg, 1.0 mol) and 6-ethoxy-pyridin-3-yl amine (140 mg, 1.0 mmol) reacted to give 6-(6-Ethoxy-pyridin-3-yl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a pale yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.04 (s, 1H), 7.41

(d, 1H), 6.93 (d, 1H), 4.46 (q, 1H), 2.80 (s, 6H), 2.45 (s, 6H), 1.46 (t, 3H); MS (ESI) 297 $(M + H)^+$.

EXAMPLE 55

6-(5-Ethoxy-pyrazin-2-yl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine

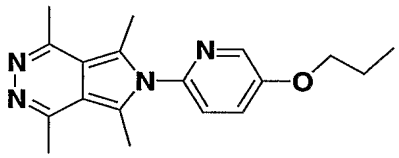
Utilizing the general procedure outlined in **Example 48,** 1,1,2,2-



tetraacetylethane (200 mg, 1.0 mol) and 5-ethoxy-pyrazin-2-yl amine (130 mg, 1.0 mmol) reacted to give 6-(5-ethoxy-pyrazin-2-yl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as light yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.27 (s, 1H), 8.11 (s, 1H), 4.50 (q, 1H), 2.80 (s, 6H), 2.48 (s, 6H), 1.50 (t, 3H); MS (ESI) 298 $(M + H)^+$.

EXAMPLE 56

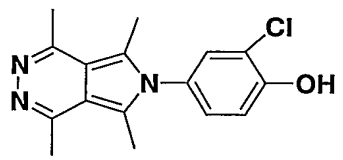
1,4,5,7-Tetramethyl-6-(5-propoxy-pyridin-2-yl)-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **Example 48,** 1,1,2,2-tetraacetylethane (100 mg, 0.5 mol) and 5-ethoxy-pyrazin-2-yl amine (80 mg, 0.5 mmol) reacted to give 1,4,5,7-tetramethyl-6-(5-propoxy-pyridin-2-yl)-6*H*-pyrrolo[3,4-*d*]pyridazine as yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.35 (s, 1H), 7.44 (d, 1H), 7.22 (d, 1H), 4.08 (t, 2H), 2.80 (s, 6H), 2.45 (s, 6H), 1.89 (q, 2H), 1.10 (t, 3H); MS (ESI) 311 $(M + H)^+$.

EXAMPLE 57

2-Chloro-4-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-phenol

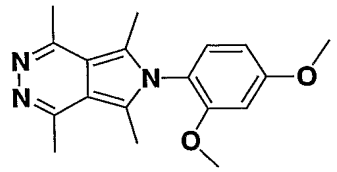


Utilizing the general procedure outline in **Example 48,** 1,1,2,2-tetraacetylethane (200 mg, 1.0 mol) and 4-amino-2-chloro-phenol amine (144 mg, 1.0 mmol) reacted to give 1-[4-acetyl-1-(3-chloro-4-hydroxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone as yellow solid: MS (ESI) 306$(M + H)^+$.

To a solution of 1-[4-acetyl-1-(3-chloro-4-hydroxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (340 mg, 1.0 mmol) was added hydrazine (50 μL). After stirring at rt for 1 h, the reaction mixture was poured into ice water (25 mL). The resulting precipitate was filtered, washed with diethyl ether (20 mL), and then dried under vacuum to afford 2-chloro-4-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-phenol as a pale yellow solid: ^{1}H NMR (CD_3OD, 500 MHz) δ 7.34 (br s, 1H), 7.08 (m, 2H), 2.83 (s, 6H), 2.52 (s, 6H); MS (ESI) 302 $(M + H)^+$.

EXAMPLE 58

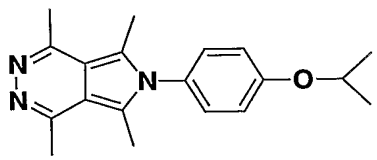
6-(2,4-Dimethoxy-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **Example 48**, 1,1,2,2-tetraacetylethane (400 mg, 2.0 mol), 2,4-dimethoxyaniline (305 mg, 2.0 mmol) and hydrazine (200 μL) reacted to give 1,4,5,7-tetramethyl-6-(4-propoxy-phenyl)-6*H*-pyrrolo[3,4-*d*]pyridazine as yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.06 (d, 1H), 6.67 (m, 2H), 3.89 (s, 3H), 3.78 (s, 3H), 2.80 (s, 6H), 2.40 (s, 6H); MS (ESI) 312 $(M + H)^+$.

EXAMPLE 59

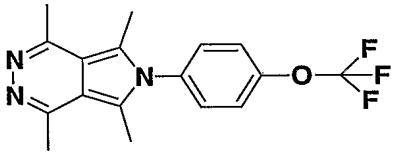
6-(4-Isopropoxy-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **Example 48**, 1,1,2,2-tetraacetylethane (100 mg, 0.5 mol), 2,4-dimethoxyaniline (76 mg, 0.5 mmol) and hydrazine (50 μL) reacted to give 6-(4-Isopropoxy-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.12 (d, 2H), 7.07 (d, 2H), 4.68 (m, 1H), 2.86 (s, 6H), 2.47 (s, 6H), 1.45 (d, 6H); MS (ESI) 310 (M + H)$^+$.

EXAMPLE 60

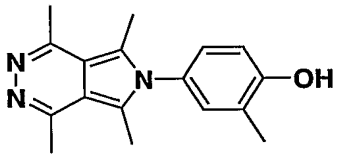
1,4,5,7-Tetramethyl-6-(4-trifluoromethoxy-phenyl)-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **Example 48,** 1,1,2,2-tetraacetylethane (200 mg, 1.0 mol), 2-methyl-4-(trifluoromethoxy) aniline (191 mg, 1.0 mmol) and hydrazine (50 μL) reacted to give 1,4,5,7-Tetramethyl-6-(4-trifluoromethoxy-phenyl)-6*H*-pyrrolo[3,4-*d*]pyridazine as light yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.27 (s, 1H), 8.11 (s, 1H), 4.50 (q, 1H), 2.80 (s, 6H), 2.48 (s, 6H), 1.50 (t, 3H); MS (ESI) 298 (M + H)$^+$; MS (ESI) 350 (M + H)$^+$.

EXAMPLE 61

2-Methyl-4-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-phenol



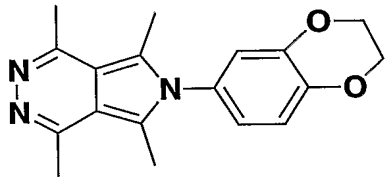
Utilizing the general procedure outlined in **Example 48**, 1,1,2,2-tetraacetylethane (400 mg, 2.0 mol) and 4-amino-*o*-cresol (250 mg, 2.0 mmol) reacted to give 1-[4-acetyl-1-(4-hydroxy-3-methyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone as yellow solid: MS (ESI) 286 (M + H)$^+$.

To a solution of 1-[4-acetyl-1-(4-hydroxy-3-methyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (100 mg, 0.32 mmol) in ethanol (5 mL) was added hydrazine (20 μL). After stirring at rt for 1 h, the reaction mixture was poured into ice

water (25 mL). The resulting precipitate was filtered, washed with diethyl ether (20 mL), and then dried under vacuum to afford 2-methyl-4-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-phenol as a pale yellow solid: ^{1}H NMR (CD_3OD, 500 MHz) δ 7.09 (d, 1H), 7.03 (s, 1H), 6.97 (d, 1H), 3.00 (s, 6H), 2.59 (s, 6H), 2.34 (s, 3H); MS (ESI) 282 $(M + H)^+$.

EXAMPLE 62

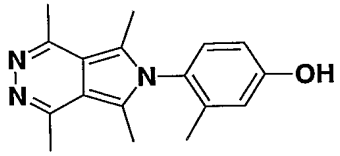
6-(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **Example 48,** 1,1,2,2-tetraacetylethane (200 mg, 1.0 mol), 5-ethoxy-pyrazin-2-yl amine (151 mg, 1.0 mmol) and hydrazine (50 μL) reacted to give 6-(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as light yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.06 (d, 1H), 6.76 (s, 1H), 6.70 (d, 1H), 4.36 (br m, 4H), 2.83 (s, 6H); MS (ESI) 310 $(M + H)^+$.

EXAMPLE 63

3-Methyl-4-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-phenol

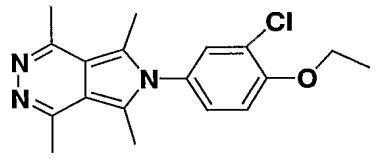


Utilizing the general procedure outlined in **Example 48,** 1,1,2,2-tetraacetylethane (200 mg, 1.0 mol) and 4-amino-3-methyl-phenol (123 mg, 1.0 mmol) reacted to give 1-[4-acetyl-1-(4-hydroxy-2-methyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone as a brown solid: MS (ESI) 306$(M + H)^+$.

Utilizing the general procedure outlined in **Example 48**, 1-[4-acetyl-1-(3-chloro-4-hydroxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (323 mg, 1.0 mmol) and hydrazine (50 μL) reacted to afford 3-methyl-4-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-phenol as brown solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.34 (br s, 1H), 7.08 (m, 2H), 2.83 (s, 6H), 2.52 (s, 6H); MS (ESI) 302 $(M + H)^+$.

EXAMPLE 64

6-(3-Chloro-4-ethoxy-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine

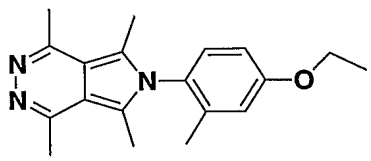


To a solution of 1-[4-acetyl-1-(3-chloro-4-hydroxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (prepared as outline in **Example 57**; 80 mg, 0.27 mmol) in 3 mL of dry DMF was added bromoethane (54 mg, 0.5 mmol) and K_2CO_3 powder (50 mg). The resulting reaction mixture was warmed to 50 °C and stirred for 1 h. It was quenched by addition of 20 mL of H_2O, extracted with diethyl ether (20 mL x 2). The combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford 1-[4-acetyl-1-(3-chloro-4-ethoxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone: MS (ESI) 302 $(M + H)^+$.

Utilizing the general procedure outlined in **Example 48**, 1-[4-acetyl-1-(3-chloro-4-ethoxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone and hydrazine reacted to give 6-(3-Chloro-4-ethoxy-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as yellow solid: ^{1}H NMR (CDOD, 500 MHz) δ 7.47 (s, 1H), 7.32 (d, 1H), 7.25 (d, 1H), 4.27 (q, 2H), 2.79 (s, 6H), 2.48 (s, 6H), 1.53 (t, 3H); MS (ESI) 330 $(M + H)^+$.

EXAMPLE 65

6-(4-Ethoxy-2-methyl-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine

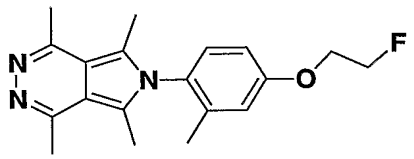


To a solution of 1-[4-acetyl-1-(4-hydroxy-2-methyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (prepared as outline in **Example 63**; 56 mg, 0.20 mmol) in 2 mL of dry DMF was added bromoethane (100 μL) and K_2CO_3 powder (50 mg). The resulting reaction mixture was warmed to 50 °C and stirred for 1 h. It was quenched by addition of 20 mL of H_2O, extracted with diethyl ether (20 mL x 2). The combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford 1-[4-acetyl-1-(4-ethoxy-2-methyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone: MS (ESI) 314 $(M + H)^+$.

Utilizing the general procedure outlined in **Example 48,** 1-[4-acetyl-1-(4-ethoxy-2-methyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone and hydrazine reacted to give 6-(4-ethoxy-2-methyl-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as light yellow solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.06 (d, 1H), 6.94 (s, 1H), 6.90 (m, 1H), 4.12 (q, 2H), 2.81 (s, 6H), 2.38 (s, 6H),1.80 (s, 3H), 1.50 (t, 3H); MS (ESI) 310 $(M + H)^+$.

EXAMPLE 66

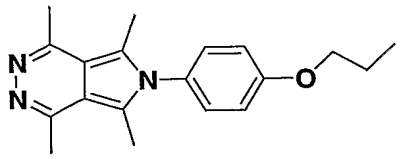
6-[4-(2-Fluoro-ethoxy)-2-methyl-phenyl]-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



As outlined in **Example 65**, 1-[4-acetyl-1-(4-hydroxy-2-methyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (20 mg) reacted with 1-bromo-2-fluoro ethane (50 μL), in the presence of K_2CO_3 powder (50 mg), to afford 1-{4-acetyl-1-[4-(2-fluoro-ethoxy)-2-methyl-phenyl]-2,5-dimethyl-1*H*-pyrrol-3-yl}-ethanone: MS (ESI) 332 $(M + H)^+$. Utilizing the general procedure outlined in **Example 48,** 1-[4-acetyl-1-(4-ethoxy-2-methyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone and hydrazine reacted to give 6-[4-(2-fluoro-ethoxy)-2-methyl-phenyl]-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as light yellow solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.06 (d, 1H), 6.94 (s, 1H), 6.90 (m, 1H), 4.12 (q, 2H), 2.81 (s, 6H), 2.38 (s, 6H),1.80 (s, 3H), 1.50 (t, 3H); MS (ESI) 310 $(M + H)^+$.

EXAMPLE 67

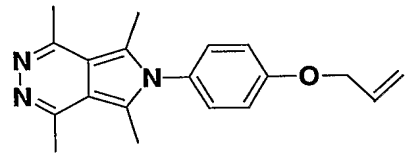
1,4,5,7-Tetramethyl-6-(4-propoxy-phenyl)-6*H*-pyrrolo[3,4-*d*]pyridazine



As outlined in **Example 65**, 1-[4-acetyl-1-(4-hydroxy-2-methyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (**Example 52**, 20 mg) reacted with 1-bromo-propane (100 μL), in the presence of K_2CO_3 powder (50 mg), to afford 1-[4-acetyl-2,5-dimethyl-1-(4-propoxy-phenyl)-1*H*-pyrrol-3-yl]-ethanone: MS (ESI) 328 $(M + H)^+$. Utilizing the general procedure outlined in **Example 48,** 1-[4-acetyl-2,5-dimethyl-1-(4-propoxy-phenyl)-1*H*-pyrrol-3-yl]-ethanone and hydrazine reacted to give 1,4,5,7-Tetramethyl-6-(4-propoxy-phenyl)-6*H*-pyrrolo[3,4-*d*]pyridazine as light yellow solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.04 (d, 1H), 6.95 (br s, 1H), 6.91 (d, 1H), 4.03 (t, 2H), 2.85 (s, 6H), 2.42 (s, 6H), 1.86 (q, 2H), 1.79 (s, 3H), 1.09 (t, 3H); MS (ESI) 328 $(M + H)^+$.

EXAMPLE 68

6-(4-Allyloxy-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*] pyridazine

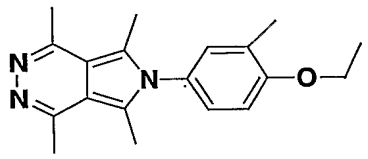


As in **Example 65**, 1-[4-acetyl-1-(4-hydroxy-2-methyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (**Example 52**, 20 mg) reacted with allyl bromide (50 μL), in the presence of K_2CO_3 (50 mg), to afford 1-[4-acetyl-1-(4-allyloxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone: MS (ESI) 326 $(M + H)^+$. Utilizing the general procedure outlined in **Example 48,** 1-[4-acetyl-1-(4-allyloxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (20 mg) and hydrazine (50 μL) reacted to give 6-(4-allyloxy-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as light yellow solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.04 (m, 1H), 6.98 (s, 1H), 6.94 (m, 1H), 6.13

(m, 1H), 5.52 (d, 1H), 5.39 (d, 1H), 4.64 (d, 2H), 2.81 (s, 6H), 2.35 (s, 6H), 1.84 (s, 3H); MS (ESI) 322 $(M + H)^+$.

EXAMPLE 69

6-(4-ethoxy-3-methyl-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine

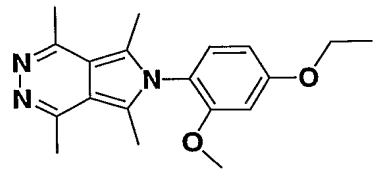


To a solution of 1-[4-acetyl-1-(4-hydroxy-3-methyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (prepared as in **Example 61**) (90 mg, 0.32 mmol) in 3 mL of dry DMF was added bromoethane (108 mg, 1.0 mmol) and K_2CO_3 powder (50 mg). The resulting reaction mixture was warmed to 50 °C and stirred for 1 h. It was quenched by addition of 20 mL of H_2O, extracted with diethyl ether (20 mL x 2). The combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford 1-[4-acetyl-1-(4-ethoxy-3-methyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone: MS (ESI) 314 $(M + H)^+$.

Utilizing the general procedure outlined in **Example 48,** 1-[4-acetyl-1-(3-chloro-4-ethoxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (99 mg, 0.32 mmol) and hydrazine (50 µL) reacted to give 6-(4-ethoxy-3-methyl-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as yellow solid: ^1H NMR (CDOD, 500 MHz) δ 6.96 (m, 3H), 4.15 (q, 2H), 2.80 (s, 6H), 2.49 (s, 6H), 2.32 (s, 3H), 1.52 (t, 3H); MS (ESI) 310 $(M + H)^+$.

EXAMPLE 70

6-(4-Ethoxy-2-methoxy-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **Example 48**, 1,1,2,2-tetraacetylethane (400 mg, 2.0 mol), 2, 4-dimethoxyaniline (305 mg, 2.0 mmol) reacted to give 1-[4-acetyl-1-(2,4-dimethoxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone as yellow solid: MS (ESI) 316 $(M + H)^+$.

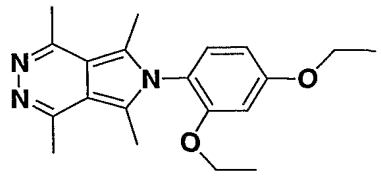
To a stirring solution of crude 1-[4-acetyl-1-(4-ethoxy-2-methoxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone prepared as above (90 mg, 0.3 mmol) in 5.0 mL of CH_2Cl_2 at 0 °C was added BBr_3 (1.0 M in CH_2Cl_2, 0.9 mL, 0.9 mmol). After 1h at 0 °C, it was warmed to rt and stirred for an additional 2 h before it was quenched with saturated aq. $NaHCO_3$ solution (5 mL). It was extracted with EtOAc (2 x 10 mL), and the combined organic extracts were washed with dried with $MgSO_4$, filtered, and concentrated *in vacuo* to afford the crude product as a yellow oil. This crude material was purified by automated chromatography on silica gel (using 20-50%EtOAc/hexanes gradient) to give the major product 1-[4-acetyl-1-(4-hydroxy-2-methoxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone as pale yellow oil: MS (ESI) 302 $(M + H)^+$; In this reaction, small amount (~10%) of minor product 1-[4-acetyl-1-(2,4-dihydroxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone was also isolated as clear colorless oil: MS (ESI) 288 $(M + H)^+$.

Utilizing the general procedure outlined in **Example 65**, 1-[4-acetyl-1-(4-hydroxy-2-methoxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (70 mg, 2.3 mmol) reacted with bromoethane (300 μL, excess), in the presence of K_2CO_3 (50 mg), to afford 1-[4-acetyl-1-(4-ethoxy-2-methoxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone: MS (ESI) 330 $(M + H)^+$.

Utilizing the general procedure outlined in **Example 48,** 1-[4-acetyl-1-(4-ethoxy-2-methoxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (60 mg) and hydrazine (50 μL) reacted to give 6-(4-Ethoxy-2-methoxy-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as light yellow solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.06 (d, 1H), 6.66 (m, 2H), 4.05 (q, 2H), 3.86 (s, 3H), 2.84 (s, 6H), 2.41 (s, 6H), 1.25 (t, 3H); MS (ESI) 326 $(M + H)^+$

EXAMPLE 71

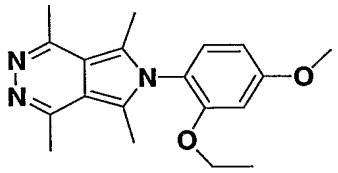
6-(2,4-diethoxy-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



Utilizing the general procedure outlined in **Example 65**, 1-[4-acetyl-1-(2,4-dihydroxy -phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone prepared as in **Example 70** (12 mg, 0.4 mmol) reacted with bromoethane (30 μL, excess), in the presence of K_2CO_3 (10 mg), to afford 1-[4-acetyl-1-(2,4-diethoxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone: MS (ESI) 344 $(M + H)^+$. Utilizing the general procedure outlined in **Example 48**, 1-[4-acetyl-1-(2,4-diethoxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (4 mg) and hydrazine (5 μL) reacted to give 6-(2,4-diethoxy-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as off-white solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.03 (d, 1H), 6.67 (s, 1H), 6.64 (d, 1H), 4.15 (q, 1H), 4.04 (q, 1H), 2.89 (br s, 6H), 2.43 (s, 6H), 1.49 (t, 3H0, 1.26 (t, 3H); MS (ESI) 340 $(M + H)^+$.

EXAMPLE 72

6-(2-ethoxy-4-methoxy-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



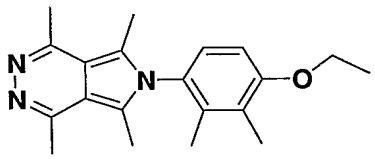
To a stirring solution of 1-[4-acetyl-1-(2,4-dimethoxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone prepared as in **Example 70** (1580 mg, 0.5 mmol) in 2.0 mL of dry DMF at rt was added sodium ethanethiolate (80%, Aldrich; 210 mg, 2.0 mmol). After 20 min at rt, it was heated to 120 °C and stirred for an additional 2 h before it was quenched with 1N HCl (5 mL). It was extracted with EtOAc (2 x 10 mL), and the combined organic extracts were washed with dried with $MgSO_4$, filtered, and concentrated *in vacuo* to afford the crude product as a yellow oil. This crude material was purified by automated chromatography on silica gel (using an 20-50% EtOAc/hexanes gradient) to give the major product 1-[4-acetyl-1-(2-hydroxy-4-

methoxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone as pale yellow oil: MS (ESI) 302 $(M + H)^+$.

Utilizing the general procedure outlined in **Example 65**, 1-[4-acetyl-1-(2-hydroxy-4-methoxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (70 mg, 2.3 mmol) reacted with bromoethane (300 μL, excess), in the presence of K_2CO_3 (50 mg), to afford 1-[4-acetyl-1-(2-ethoxy-4-methoxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone: MS (ESI) 330 $(M + H)^+$. Utilizing the general procedure outlined in **Example 48,** 1-[4-acetyl-1-(4-ethoxy-2-methoxy-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (60 mg) and hydrazine (50 μL) reacted to give 6-(2-ethoxy-4-methoxy-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as light yellow solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.04 (d, 1H), 6.68 (s, 1H), 6.64 (d, 1H), 4.15 (q, 1H), 3.78 (s, 3H), 2.81 (s, 6H), 2.40 (s, 6H), 1.51 (t, 3H); MS (ESI) 326 $(M + H)^+$.

EXAMPLE 73

6-(4-Ethoxy-2,3-dimethyl-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



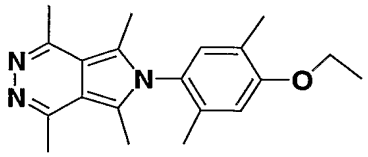
Utilizing the general procedure outlined in **Example 48,** 1,1,2,2-tetraacetylethane (300 mg, 1.5mol) and 4-amino-2.3-xylenol (206 mg, 1.5 mmol) reacted to give 1-[4-acetyl-1-(4-hydroxy-2,3-dimethyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone as yellow solid: MS (ESI) 300$(M + H)^+$.

Utilizing the general procedure outlined in **Example 65**, 1-[4-acetyl-1-(4-hydroxy-2,3-dimethyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (100 mg, 0.3 mmol) reacted with bromoethane (300 μL, excess), in the presence of K_2CO_3 (50 mg), to afford 1-[4-acetyl-1-(4-ethoxy-2,3-dimethyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone: MS (ESI) 328 $(M + H)^+$. Utilizing the general procedure outlined in **Example 48,** 1-[4-acetyl-1-(4-ethoxy-2,3-dimethyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (108 mg, 0.3) and hydrazine (50 μL) reacted to give 6-(4-Ethoxy-2,3-dimethyl-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as off-white solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 6.92 (d, 1H), 6.86(d, 1H), 4.14 (q, 2H), 2.83 (s, 6H), 2.36 (s, 6H), 2.28 (s, 3H), 1.72 (s, 3H), 1.52 (t, 3H); MS (ESI) 324 $(M + H)^+$.

EXAMPLE 74

6-(4-Ethoxy-2,5-dimethyl-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine

Utilizing the general procedure outlined in **Example 481,** 1,1,2,2-

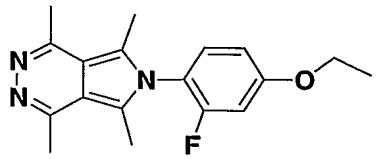


tetraacetylethane (200 mg, 1.0 mol) and 4-amino-2.5-dimethylphenol (138 mg, 1.0 mmol) reacted to give 1-[4-acetyl-1-(4-hydroxy-2,5-dimethyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone as yellow solid: MS (ESI) 300 $(M + H)^+$.

Utilizing the general procedure outlined in **Example 7**, 1-[4-acetyl-1-(4-hydroxy-2,5-dimethyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (100 mg, 0.3 mmol) reacted with bromoethane (300 μL, excess), in the presence of K_2CO_3 (50 mg), to afford 1-[4-acetyl-1-(4-ethoxy-2,5-dimethyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone: MS (ESI) 328 $(M + H)^+$. Utilizing the general procedure outlined in **Example 48,** 1-[4-acetyl-1-(4-ethoxy-2,5-dimethyl-phenyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-ethanone (108 mg, 0.3) and hydrazine (50 μL) reacted to give 6-(4-Ethoxy-2,3-dimethyl-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]-pyridazine as an off-white solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 6.88 (s, 1H), 6.77 (s, 1H), 4.14 (q, 2H), 2.85 (s, 6H), 2.39 (s, 6H), 2.26 (s, 3H), 1.83 (s, 3H, 1.50 (t, 3H); MS (ESI) 324 $(M + H)^+$.

EXAMPLE 75

6-(4-Ethoxy-2-fluoro-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



To a solution of 3-fluoro-4-nitrophenol (1.57 g, 10.0 mmol) in 20 mL of dry DMF was added bromoethane (540 mg, 5.0 mmol) and K_2CO_3 powder (500 mg). The resulting reaction mixture was warmed to 50 °C and stirred for 1 h. It was quenched

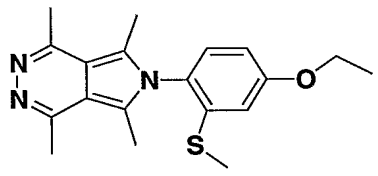
by addition of 20 mL of H_2O, extracted with diethyl ether (100 mL x 2). The combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford 4-ethoxy-2-fluoro-1-nitrobenzene as a pale yellow oil: MS (ESI) 186 $(M + H)^+$.

To a solution of 4-ethoxy-2-fluoro-1-nitro benzene (1.0 g, 5.4 mmol) in absolute EtOH (25 mL) at rt was added 250 mg of Pd/C (Aldrich, 10 wt.% on activated carbon), followed by slow addition of hydrazine hydrate (2.5 mL). The resulting reaction mixture was refluxed at 90 °C for 30 min. It then cooled to rt, filtered through Celite, and then concentrated *in vacuo* to afford 4-ethoxy-2-fluoro-phenyl amine as a pale yellow oil: MS (ESI) 156 $(M + H)^+$.

Utilizing the general procedure outlined in **Example 48,** 1,1,2,2-tetraacetylethane (200 mg, 1.0 mol), 4-ethoxy-2-fluoro-phenyl amine (155 mg, 1.0 mmol) and hydrazine (50 μL) reacted to give 6-(4-ethoxy-2-fluoro-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as yellow solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.13 (t, 1H), 6.88 (m, 2H), 4.16 (q, 2H), 2.82 (s, 6H), 2.46 (s, 6H), 1.53 (t, 3H); MS (ESI) 314 $(M + H)^+$.

EXAMPLE 76

6-(4-Ethoxy-2-methylsulfanyl-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-d]pyridazine



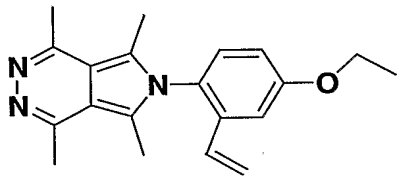
To a solution of 4-Ethoxy-2-fluoro-1-nitro benzene prepared as in **Example 75** (185 mg, 1.0 mmol) in 2 mL of dry DMF was added NaSMe (84 mg, 1.20 mmol). The resulting reaction mixture was warmed to 50 °C and stirred for 1 h. It was quenched by addition of 20 mL of H_2O. The precipitate was filtered, washed with H_2O and dried under vacuum to afford 4-ethoxy-2-methylsulfanyl-1-nitro-benzene as yellow oil: MS (ESI) 211 $(M + H)^+$.

To a solution of 4-ethoxy-2-methylsulfanyl-1-nitro-benzene (1.0 g, 5.4 mmol) in absolute EtOH (25 mL) at rt was added 40 mg of Pd/C (Aldrich, 10 wt.% on active carbon), followed by slow addition of hydrazine hydrate (0.5 mL). The resulting reaction mixture was refluxed at 90 °C for 3 h. It then cooled to rt, filtered through Celite, and then concentrated *in vacuo* to afford 4-ethoxy-2-methylsulfanyl-phenyl amine as a pale yellow oil: MS (ESI) 184 $(M + H)^+$.

Utilizing the general procedure outlined in **Example 48,** 1,1,2,2-tetraacetylethane (200 mg, 1.0 mol), 4-ethoxy-2-methylsulfanyl-phenyl amine (140 mg, 0.8 mmol) and hydrazine (50 μL) reacted to give 6-(4-Ethoxy-2-methylsulfanyl-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-d]pyridazine as yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.05 (d, 1H), 6.88 (s, 1H), 6.82 (d, 1H), 4.16 (q, 2H), 2.81 (s, 6H), 2.42 (s, 6H), 1.53 (t, 3H); MS (ESI) 342 $(M + H)^+$.

EXAMPLE 77

6-(4-Ethoxy-2-vinyl-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



To a solution of 3-hydroxymethyl-4-nitro-phenol (510 mg, 3.0 mmol) in 5 mL of dry DMF was added bromoethane (540 mg, 5.0 mmol) and K_2CO_3 powder (500 mg). The resulting reaction mixture was warmed to 50 °C and stirred for 1 h. It was quenched by addition of 20 mL of H_2O, extracted with diethyl ether (2 x 20 mL). The combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford (5-ethoxy-2-nitro-phenyl)-methanol as a pale yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.20 (d, 1H), 7.36 (s, 1H), 6.89 (m, 1H), 5.00(s, 2H), 4.16(q, 2H), 2.57 (br t, 1H), 1.49 (t, 3H).

To a solution of (5-ethoxy-2-nitro-phenyl)-methanol (592 mg, 3.0 mmol) in absolute EtOH (20 mL) at rt was added 150 mg of Pd/C (Aldrich, 10 wt.% on active carbon), followed by slow addition of hydrazine hydrate (1.5 mL). The resulting reaction mixture was refluxed at 90 °C for 1h. It was then cooled to rt,

filtered through Celite, and then concentrated *in vacuo* to afford crude (2-amino-5-ethoxy-phenyl)-methanol as a pale yellow oil: MS (ESI) 168 $(M + H)^+$.

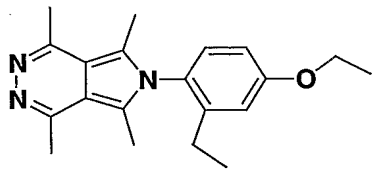
A solution of 1,1,2,2-tetraacetylethane (600 mg, 3.0 mol) and (2-amino-5-ethoxy-phenyl)-methanol (496 mg, 3.0 mmol) was refluxed in EtOH (10 mL)/AcOH (1%) for 14 h. It was cooled to rt, and anhydrous hydrazine (200 μL, 6.3 mmol) was added. After stirring at rt for 1 h, the reaction mixture was poured into ice water (50 mL). The resulting precipitate was filtered, washed with diethyl ether (20 mL), and then dried under vacuum to afford [5-ethoxy-2-(1,4,5,7-tetramethyl-pyrrolo[3,4-δ]pyridazin-6-yl)-phenyl]-methanol as a pale yellow solid: ^{1}H NMR ($CDCL_3$, 500 MHz) δ 7.24 (s, 1H), 6.98(m, 2H), 4.62 (s, 2H), 4.16 (q, 2H), 2.66 (s, 6H), 2.41 (s, 6H), 1.50 (t, 3H); MS (ESI) 327 $(M + H)^+$.

. To a solution of [5-ethoxy-2-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-phenyl]-methanol (70 mg, 2.3 mmol) in CH_2Cl_2 (10 mL) at rt was added MnO_2 (200 mg, excess). The resulting reaction mixture was stirred at rt for 2 h before if was filtered through Celite, and eluted with CH_2Cl_2 (20mL x 2). The eluant was collected and concentrated *in vacuo* to afford 5-ethoxy-2-(1,4,5,7-tetramethyl-pyrrolo[3,4-δ]pyridazin-6-yl)-benzaldehyde as a yellow soild: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.56 (s, 1H), 7.71 (s, 1H), 7.40 (d, 1H), 7.20 (d, 1H), 4.28 (q, 2H), 2.86 (s, 6H), 2.45 (s, 6H), 1.58 (t, 3H); MS (ESI) 325 $(M + H)^+$.

A suspension of methyltriphenylphosphonium bromide (178 mg, 0.5 mmol) in 3.0 mL of THF at rt was treated with *n*-BuLi (1.6 **M** in Hexane, 280 μL, 0.45 mmol) dropwise. After 5 min at rt, it was warmed to 50 °C and stirred for 30 min, and then cooled back to rt to give the *in situ* generated ylide solution. Part of this reaction solution (2.0 mL) was transferred to another reaction flask containing 5-ethoxy-2-(1,4,5,7-tetramethyl-pyrrolo[3,4-δ]pyridazin-6-yl)-benzaldehyde (32 mg, 0.1 mol) and 0.5 mL of THF under N_2 atmosphere. The resulting reaction mixture was stirred at rt for 3h before it was quenched with H_2O and extracted with diethyl ether (2 x 10 mL). All organic extracts were combined, dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford crude product as yellow oil. It was purified by preparative TLC plate (20 x 20 cm, 0.5 mm layer thickness, eluted with 7% CH_2Cl_2/MeOH) to give pure 6-(4-ethoxy-2-vinyl-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-δ]pyridazine as a pale yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.26 (s, 1H), 7.06 (d, 1H), 6.98 (d, 1H), 5.79 (dd, 1H), 5.77 (d, 1H), 5.24 (d, 2H), 4.15 (q, 2H), 2.81 (s, 6H), 2.37 (s, 6H), 1.52 (t, 3H), ; MS (ESI) 323 $(M + H)^+$.

EXAMPLE 78

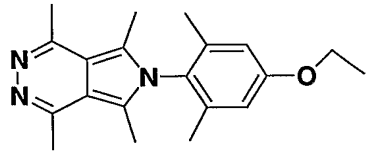
6-(4-Ethoxy-2-ethyl-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



To a solution of 6-(4-ethoxy-2-vinyl-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine (30 mg, 3.0 mmol) in 3 mL of ethanol was added anhydrous hydrazine (20 μL). The resulting reaction solution was refluxed at 90 °C for 90 min. It was allowed to warm to rt and directly condensed *in vacuo* to afford 6-(4-Ethoxy-2-ethyl-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a light yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.00 (m, 2H), 6.89 (m, 1H), 4.15 (q, 2H), 2.82 (s, 6H), 2.38 (s, 6H), 2.10 (q, 2H), 1.52 (t, 3H), 1.08 (t, 3H); MS (ESI) 324 $(M + H)^+$.

EXAMPLE 79

6-(4-Ethoxy-2,6-dimethyl-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



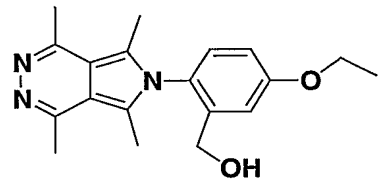
Utilizing the general procedure outlined in **Example 77**, 4-nitro-3,5-dimethyl-phenol was converted to 4-ethoxy-2,6-dimethyl-phenylamine in two step. This crude amine was use directly in the next reaction without further purification.

Utilizing the general procedure outlined in **Example 48,** 1,1,2,2-tetraacetylethane (308 mg, 1.56 mol), 4-ethoxy-2,6-dimethyl-phenylamine (250 mg, 1.0 mmol) and hydrazine (100 μL) reacted to give 6-(4-ethoxy-2,6-dimethyl-phenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]-pyridazine as yellow solid: ^{1}H NMR ($CDCl_3$,

500 MHz) δ 6.81 (s, 1H), 6.75 (s, 1H), 4.04 (q, 2H), 2.82 (s, 6H), 2.44 (s, 6H), 2.47 (s, 3H), 2.35 (s, 6H), 1.79 (s, 3H), 1.88 (t, 3H), ; MS (ESI) 324 $(M + H)^+$.

EXAMPLE 80

[5-Ethoxy-2-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-phenyl]-methanol



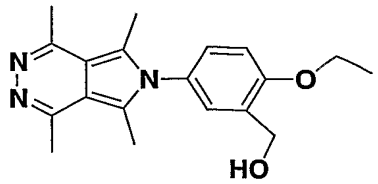
To a solution of 3-hydroxymethyl-4-nitro-phenol (510 mg, 3.0 mmol) in 5 mL of dry DMF was added bromoethane (540 mg, 5.0 mmol) and K_2CO_3 powder (500 mg). The resulting reaction mixture was warmed to 50 °C and stirred for 1 h. It was quenched by addition of 20 mL of H_2O, extracted with diethyl ether (2 x 20 mL). The combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford (5-ethoxy-2-nitro-phenyl)-methanol as a pale yellow oil: ^1H NMR ($CDCl_3$, 500 MHz) δ 8.20 (d, 1H), 7.36 (s, 1H), 6.89 (m, 1H), 5.00(s, 2H), 4.16(q, 2H), 2.57 (br t, 1H), 1.49 (t, 3H).

To a solution of (5-ethoxy-2-nitro-phenyl)-methanol (592 mg, 3.0 mmol) in absolute EtOH (20 mL) at rt was added 150 mg of Pd/C (Aldrich, 10 wt.% on activated carbon), followed by slow addition of hydrazine hydrate (1.5 mL). The resulting reaction mixture was refluxed at 90 °C for 1h. It then cooled to rt, filtered through Celite, and then concentrated *in vacuo* to afford crude (2-amino-5-ethoxy-phenyl)-methanol as a pale yellow oil: MS (ESI) 168 $(M + H)^+$.

A solution of 1,1,2,2-tetraacetylethane (600 mg, 3.0 mol) and (2-amino-5-ethoxy-phenyl)-methanol (496 mg, 3.0 mmol) was refluxed in EtOH (10 mL)/AcOH (1%) for 14 h. It was cooled to rt, and anhydrous hydrazine (200 μL, 6.3 mmol) was added. After stirring at rt for 1 h, the reaction mixture was poured into ice water (50 mL). The resulting precipitate was filtered, washed with diethyl ether (20 mL), and then dried under vacuum to afford [5-ethoxy-2-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-phenyl]-methanol as a pale yellow solid: ^1H NMR ($CDCL_3$, 500 MHz) δ 7.22 (s, 1H), 6.95 (m, 2H), 4.40 (s, 2H), 4.16 (q, 2H), 2.66 (s, 6H), 2.41 (s, 6H), 1.50 (t, 3H); MS (ESI) 326 $(M + H)^+$.

EXAMPLE 81

[2-Ethoxy-5-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-phenyl]-methanol

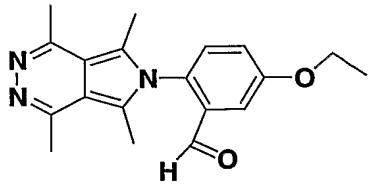


Utilizing the general procedure outlined in **Example 77**, 2-hydroxymethyl-4-nitro-phenol was converted to afford (5-amino-2-ethoxy-phenyl)-methanol in two step. This crude amine was use directly in the next reaction without further purification.

Utilizing the general procedure outlined in **Example 48,** 1,1,2,2-tetraacetylethane (308 mg, 1.56 mol), (5-amino-2-ethoxy-phenyl)-methanol (250 mg, 1.0 mmol) and hydrazine (100 μL) reacted to give [2-ethoxy-5-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-phenyl]-methanol as yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.24 (s, 1H), 7.08-7.01 (m, 2H), 4.81 (s, 2H), 4.18 (q, 2H), 2.77 (s, 6H), 2.43 (s, 6H), 1.51 (t, 3H); MS (ESI) 326 $(M + H)^+$.

EXAMPLE 82

5-Ethoxy-2-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-benzaldehyde

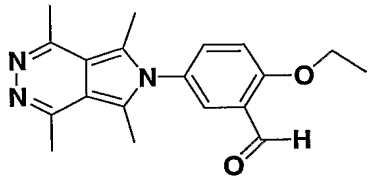


To a solution of [5-ethoxy-2-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-phenyl]-methanol (prepared as described in **Example 81**; 70 mg, 2.3 mmol) in CH_2Cl_2 (10 mL) at rt was added MnO_2 (200 mg, excess). The resulting reaction mixture was stirred at rt for 2 h before if was filtered through Celite, and eluted with CH_2Cl_2 (2 x 20mL). The eluant was collected and concentrated *in vacuo* to afford 5-

ethoxy-2-(1,4,5,7-tetramethyl-pyrrolo[3,4-δ]pyridazin-6-yl)-benzaldehyde as a yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.55 (s, 1H), 7.70 (s, 1H), 7.40 (d, 1H), 7.20 (d, 1H), 4.30 (s, 2H), 2.87 (s, 6H), 2.45 (s, 6H), 1.57 (t, 3H); MS (ESI) 324 $(M + H)^+$.

EXAMPLE 83

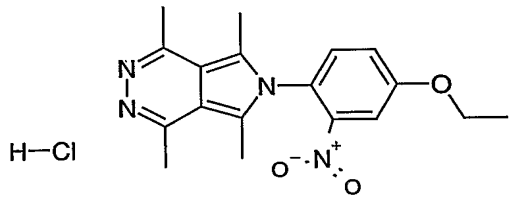
2-Ethoxy-5-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-benzaldehyde



Utilizing the general procedure outlined in **Example 82**, [5-ethoxy-2-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-phenyl]-methanol (prepared as described in **Example 81**; 100 mg, 0.3 mmol) reacted with MnO_2 (200 mg, excess) to afford 2-ethoxy-5-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-benzaldehyde as a yellow soild: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.20 (s, 1H), 7.57 (s, 1H), 7.34 (d, 1H), 7.24 (d, 1H), 4.20 (q, 2H), 2.90 (s, 6H), 2.42 (s, 6H), 1.51 (t, 3H); MS (ESI) 324 $(M + H)^+$.

EXAMPLE 84

6-(4-ethoxy-2-nitrophenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride



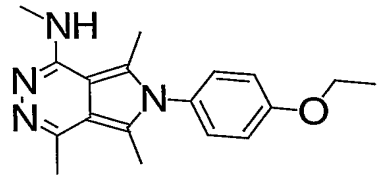
To a solution of acetonyl acetone (1.95mL, 16.5mmol) in acetic acid (100mL) was added 4-ethoxy-2-nitroaniline (3.0g, 16.5mmol) and the red mixture heated at reflux overnight. After cooling to rt, the now black solution was poured into water and extracted with EtOAc (2 x 200mL). The combined organic layers were

washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to an oil. Purification by flash chromatography (10% EtOAc/hexanes) gave 2,5-dimethyl-1-(4-ethoxy-2-nitrophenyl)pyrrole as a red oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.46 (d, 1H), 7.27 (t, 1H), 7.19 (dd, 1H), 5.91 (s, 2H), 4.15 (q, 1H), 1.96 (s, 6H), 1.50 (t, 3H); MS (ESI) 261 $(M + H)^+$.

To a solution of 2,5-dimethyl-1-(4-ethoxy-2-nitrophenyl)pyrrole (3.10g, 11.9mmol) in CH_2Cl_2 (80mL) at 0 °C was added acetyl chloride (2.13mL, 30mmol) followed by dropwise addition of tin(IV) chloride (3.51mL, 30mmol). The solution was allowed to warm to rt overnight followed by heating at reflux for an addition 24 hours. After cooling to rt, the reaction was diluted with 0.25M NaOH, extracted with EtOAc, the organic layer washed with brine, dried over $MgSO_4$, filtered, concentrated *in vacuo*, and purified by flash chromatography (20-75% EtOAc/hexanes) to give 3,4-diacetyl-2,5-dimethyl-1-(4-ethoxy-2-nitrophenyl)pyrrole as a green solid (MS (ESI) 345 $(M + H)^+$; the major product being monoacylation). The solid was taken up in ethanol (10mL), an excess of hydrazine (0.1mL) added, and the solution heated at 50°C. After 3 hours, the reaction was poured over ice, filtered, taken up in hot ether, precipitated with HCl in ether, and filtered to give 6-(4-ethoxy-2-nitrophenyl)-1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine hydrochloride as a tan solid: ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.93 (d, 1H), 7.68 – 7.61 (m, 2H), 4.29 (q, 1H), 3.02 (br s, 3H), 2.82 (br s, 3H), 2.46 (s, 6H), 1.42 (t, 3H); MS (ESI) 341 $(M + H)^+$.

EXAMPLE 85

6-(4-ethoxyphenyl)-*N*,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-amine



To a slurry of NaH (2.6g, 66mmol, 60% dispersion in mineral oil) and THF (200mL) at 0°C was added ethyl acetoacetate (7.8mL, 60mmol) dropwise. After 15min, α-chloroacetone (5.2mL, 66mmol) was added and the resulting solution allowed to warm to rt over 12h. The reaction mixture was partitioned between MTBE and water, the water layer extracted with MTBE (2 x 50mL), and the combined extracts dried ($MgSO_4$), and concentrated under reduced pressure to afford,

after automated chromatography on silica gel (using an EtOAc/hexanes gradient), ethyl 2-acetyl-4-oxopentanoate as a colorless oil.

Ethyl 2-acetyl-4-oxopentanoate (6.37g, 34.2mmol) was dissolved in 20mL of EtOH. *p*-Phenetidine (4.70g, 34.2mmol) was added as well as several drops of AcOH and heated at reflux for 15h. The reaction mixture was allowed to cool to rt and then concentrated under reduced pressure. The resulting brown oil was dissolved in CH_2Cl_2 (20mL) and washed with saturated aqueous $NaHCO_3$ (3 x 50mL) dried ($MgSO_4$) and concentrated. The resulting crude ethyl 1-(4-ethoxyphenyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate was taken on without further purification. MS (ESI) 288 $(M+H)^+$.

In an oven-dried flask, ethyl 1-(4-ethoxyphenyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (9.32g, 32.5mmol) combined with toluene (100mL), acetyl chloride (2.8mL, 39.3mmol), and $SnCl_4$ (4.67mL, 29.3mmol). The reaction mixture was stirred at rt for 4h. The reaction was quenched by the addition of 1N NaOH (added until pH 12 was reached) and the aqueous layer extracted with CH_2Cl_2 (2 x 200mL) and Et_2O (2 x 100mL). The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. The resulting crude (ethyl-4-acetyl-1-(4-ethoxyphenyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate) was of sufficient purity for further reactions. MS (ESI) 330 $(M+H)^+$.

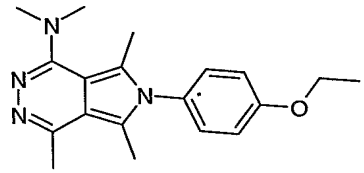
A solution of ethyl-4-acetyl-1-(4-ethoxyphenyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (7.50g, 22.8mmol) and EtOH (75mL) was placed in a resealable reaction vessel. Hydrazine (2mL, 64 mmol) and AcOH (~1mL) were added, the tube closed, and heated to 80°C for 12h. The resulting slurry was allowed to cool to rt and poured into ice water (50mL). The resulting white solid (6-(4-ethoxyphenyl)-4,5,7-trimethyl-2,6-dihydro-1*H*-pyrrolo[3,4-*d*]pyridazin-1-one) was filtered and dried under vacuum for 8 h. MS (ESI) 298 $(M+H)^+$.

A solution of $POCl_3$ (15mL) and 6-(4-ethoxyphenyl)-4,5,7-trimethyl-2,6-dihydro-1*H*-pyrrolo[3,4-*d*]pyridazin-1-one (1.5g) were combined and heated at reflux for 48h. The reaction mixture was allowed to cool to rt, and was quenched by the careful addition of water (50mL) followed by a saturated aqueous solution $NaHCO_3$ (50mL). The reaction mixture was extracted with CH_2Cl_2 (5 x 50mL), and the combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to yield 1-chloro-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a yellow/green solid. MS (ESI) 316 $(M+H)^+$.

To a *Personal Chemistry Microwave Synthesizer* microwave vial was combined 1-chloro-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine (200mg, 0.64mmol), $MeNH_2$ (1mL, 40% in H_2O), and EtOH (1mL). The vial was sealed and heated at 120°C for 12min. The reaction mixture was poured into water to afford crude 6-(4-ethoxyphenyl)-*N*,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-amine. Purification by reverse phase preparative HPLC using a YMC CombiPrep Pro C_{18} 20x100 column (Gradient:5%-100% Acetonitrile in a H_2O + 0.1% TFA solution over 10min, retention time: 6.1min) afforded pure 6-(4-ethoxyphenyl)-*N*,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-amine as a colorless solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.05-7.12 (m, 4H), 4.16 (q, 2H), 3.20 (s, 3H), 2.69 (s, 3H), 2.43 (s, 3H), 2.39 (s, 3H), 1.51 (t, 3H); MS (ESI) 311 $(M+H)^+$.

EXAMPLE 86

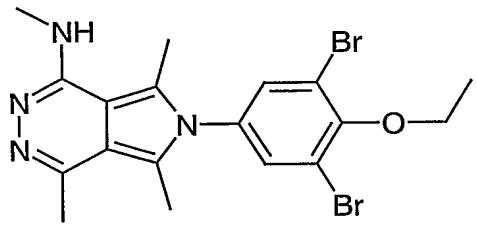
6-(4-ethoxyphenyl)-*N*,*N*,4,5,7-pentamethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-amine



Utilizing the general procedure outlined in **EXAMPLE 85**, 1-chloro-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine and Me_2N (1mL, 40% solution in H_2O) reacted to give 6-(4-ethoxyphenyl)-*N*,*N*,4,5,7-pentamethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-amine: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.06-7.15 (m, 4H), 4.15 (q, 2H), 3.08 (s, 6H), 2.78 (s, 3H), 2.50 (s, 2H), 2.44 (s, 2H), 1.51-1.52 (s, 3H); MS (ESI) 325 $(M+H)^+$.

EXAMPLE 87

6-(3,5-dibromo-4-ethoxyphenyl)-1-aminomethyl-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine

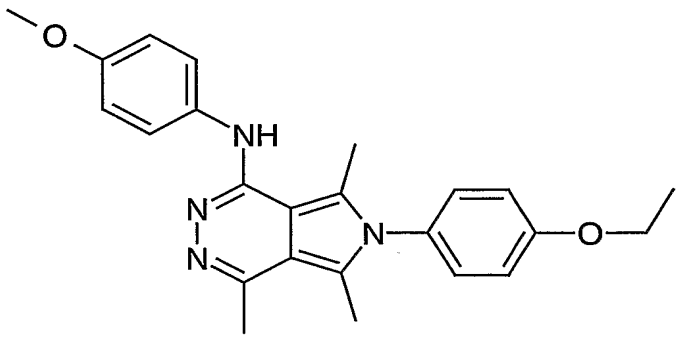


Utilizing the procedure outlined in **Example 85**, ethyl 2-acetyl-4-oxopentanoate (6.37g, 34.2mmol) was dissolved in 20mL of EtOH. 2,6-dibromo-4-aminophenol (11.6g, 34.2mmol) were reacted to afford ethyl 1-(3,5-dibromo-4-hydroxyphenyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate was taken on without further purification. MS (ESI) 418 $(M+H)^+$.

Crude ethyl 1-(3,5-dibromo-4-hydroxyphenyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate was mixed with Cs_2CO_3 (11.4 g, 35 mmol), bromoethane (7.50 g, 70.0 mmol), and MeCN (150 mL) and heated at 50 °C for 4 hr. Standard aqueous workup afforded, after purification on silica gel (utilizing an ethyl acetate/hexanes gradient) ethyl 1-(3,5-dibromo-4-ethoxyphenyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate as a reddish solid. MS (ESI) 446 $(M+H)^+$. This compound was processed as in **example 85** to afford 6-(3,5-dibromo-4-ethoxyphenyl)-*N*,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazin-1-amine as a colorless solid: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.41 (s, 2H), 4.19 (q, 2H), 3.13 (s, 3H), 2.62 (s, 3H), 2.59 (s, 3H), 2.40 (s, 3H), 1.54 (t, 3H); MS (ESI) 469 $(M+H)^+$.

EXAMPLE 88

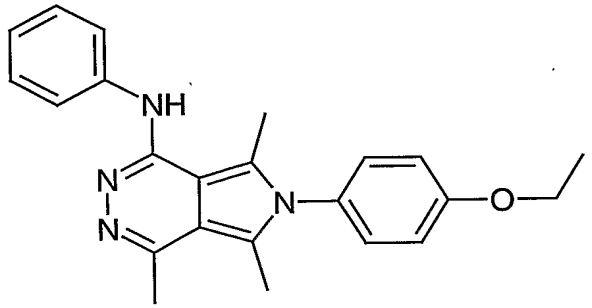
6-(4-ethoxyphenyl)-1-(4-methoxyphenyl)amino-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 85**, 1-chloro-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine and *p*-anisidine (0.40 mg, 0.32 mmol) reacted to give 6-(4-ethoxyphenyl)-1-hydrazino-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.32 (d, 2H), 7.08 (d, 2H), 7.06 (d, 2H), 6.91 (d, 2H), 4.12 (q, 2H), 3.81 (s, 3H), 2.69 (s, 3H), 2.55 (s, 3H), 1.50 (t, 3H); MS (ESI) 403 $(M+H)^+$.

EXAMPLE 89

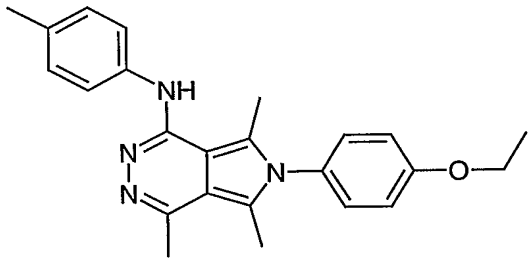
6-(4-ethoxyphenyl)-1-aminophenyl-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 85**, 1-chloro-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine and aniline (0.36 mg, 0.32 mmol) reacted to give 6-(4-ethoxyphenyl)-1-hydrazino-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.33-7.36 (m, 3H), 6.65-7.13 (m, 6H), 4.14 (q, 2H), 2.42 (s, 3H), 2.37 (s, 3H), 2.32 (s, 3H) 1.52 (t, 3H); MS (ESI) 403 $(M+H)^+$.

EXAMPLE 90

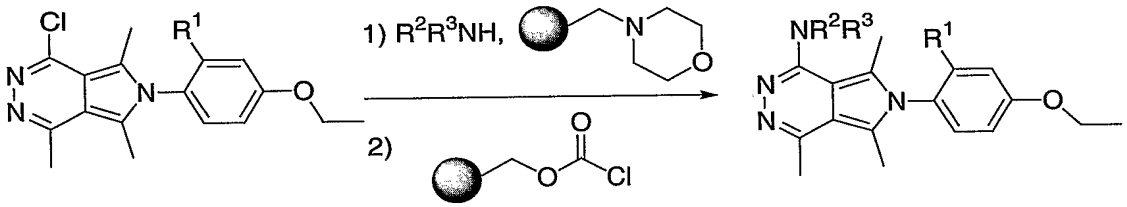
6-(4-ethoxyphenyl)-1-(4-methylphenyl)amino-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine



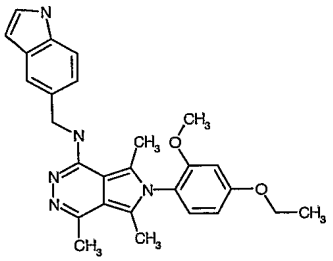
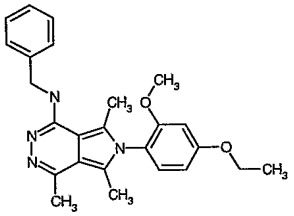
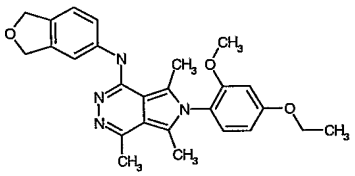
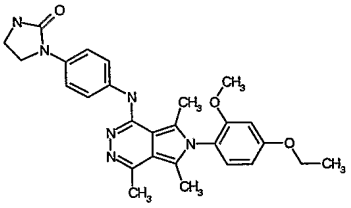
Utilizing the general procedure outlined in **EXAMPLE 85**, 1-chloro-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine and 4-methylaniline (0.40 mg, 0.32 mmol) reacted to give 6-(4-ethoxyphenyl)-1-hydrazino-4,5,7-

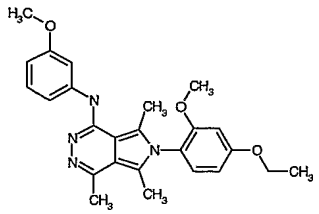
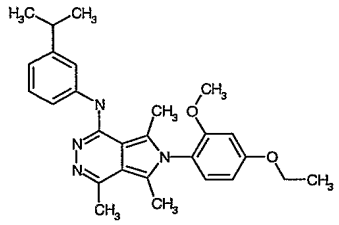
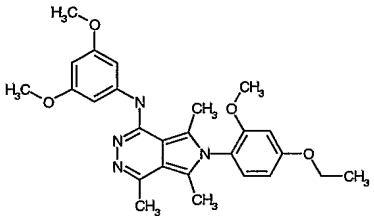
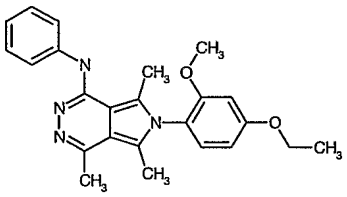
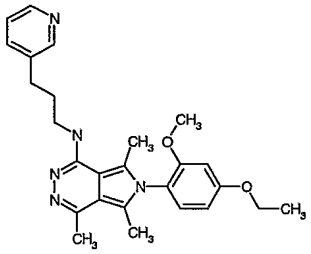
trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.50 (d, 2H), 7.17 (d, 2H), 7.16 (d, 2H), 6.99 (d, 2H), 4.16 (q, 2H), 2.81 (s, 3H), 2.34 (s, 3H), 2.27 (s, 3H), 2.21 (s, 3H), 1.52 (t, 3H); MS (ESI) 423 $(M+H)^+$.

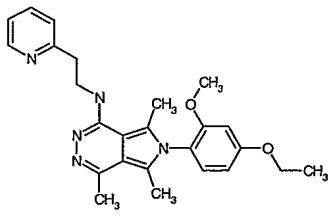
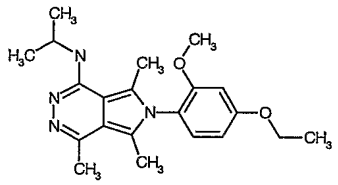
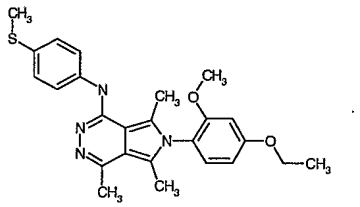
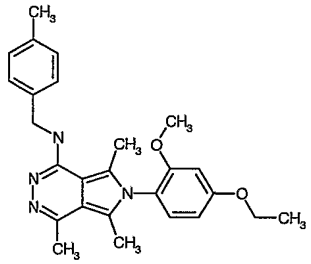
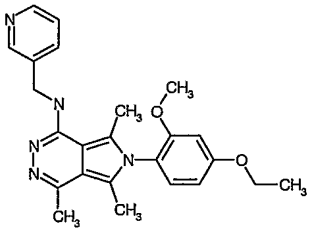
Examples 91-367

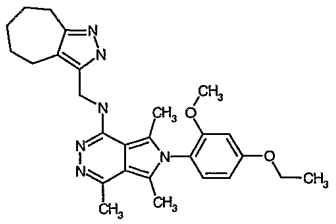
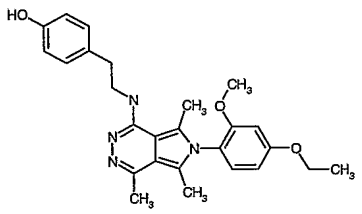
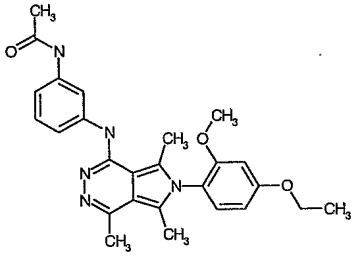
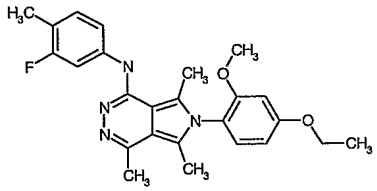
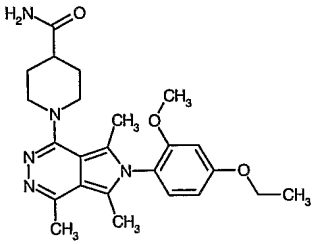


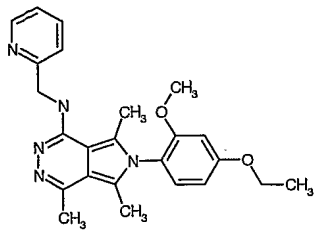
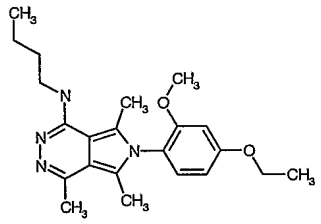
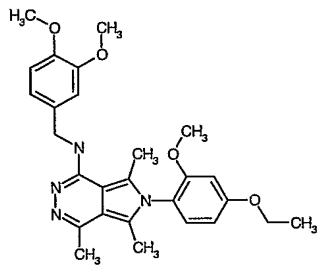
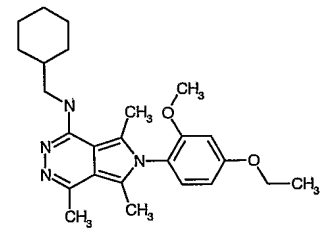
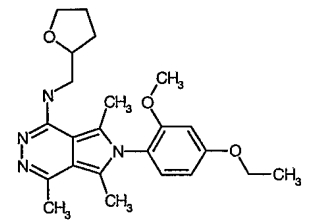
Example 91-367 were synthesized in library mode. 1-Chloro-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-d]pyridazine (50 mg per vessel) or 1-Chloro-6-(2-methoxy-4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-d]pyridazine (prepared as in example 85 utilizing 2-methoxy-4-ethoxy aniline)(50 mg per vessel), and polystyrene resin-bound *N*-methylmorpholine (1.1 eq.) were dry loaded into reaction vessels. Amines (2 eq.) in pyridine (1 mL) was added to the vessels. The vessels were capped and sealed. The reactions were heated to 100 °C and agitated overnight. Additional polystyrene resin-bound *N*-methylmorpholine (2 eq.), polystyrene resin-bound chloroformate (2 eq.), and chloroform (4 mL) were added. The resulting suspension was agitated at 50 °C overnight. The reaction solutions were collected by filtration, concentrated and dried in GeneVac. The products were analyzed by LCMS.

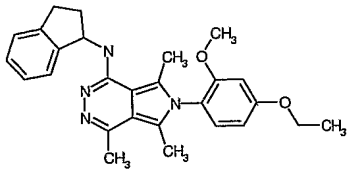
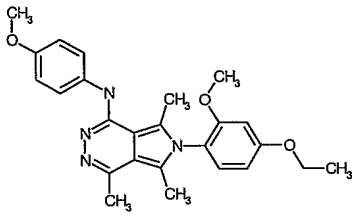
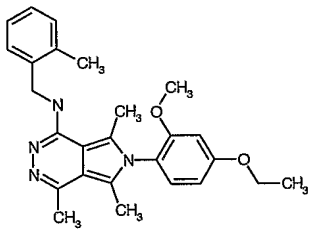
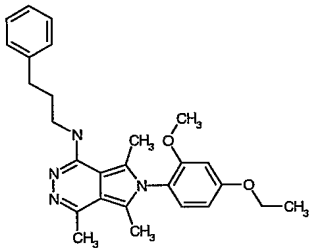
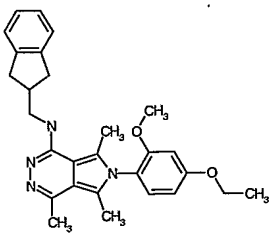
Example	Name	Structure	MS (ESI)
Example 91	6-(4-ethoxy-2-methoxyphenyl)-N-(1H-indol-5-ylmethyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		457
Example 92	N-benzyl-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		418
Example 93	N-(1,3-dihydro-2-benzofuran-5-yl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		446
Example 94	1-(4-{[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]amino}phenyl)imidazolidin-2-one		488

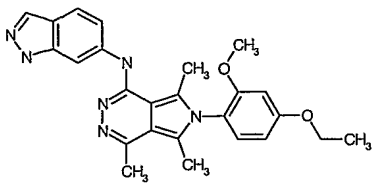
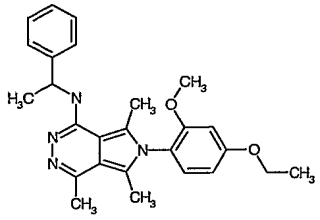
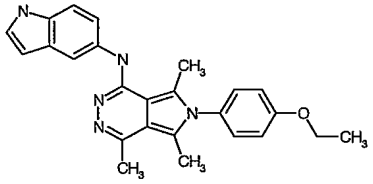
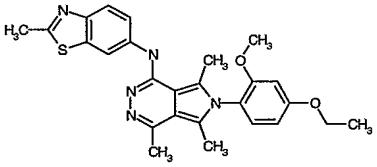
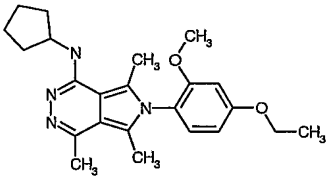
Example 95	6-(4-ethoxy-2-methoxyphenyl)-N-(3-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		434
Example 96	6-(4-ethoxy-2-methoxyphenyl)-N-(3-isopropylphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		446
Example 97	N-(3,5-dimethoxyphenyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		464
Example 98	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-phenyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		404
Example 99	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(3-pyridin-3-ylpropyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		447

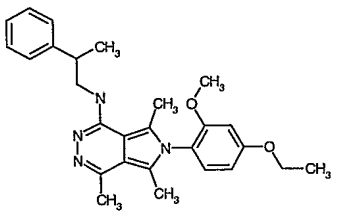
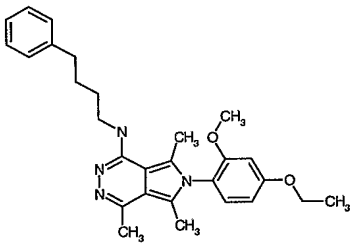
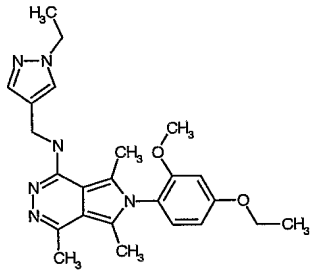
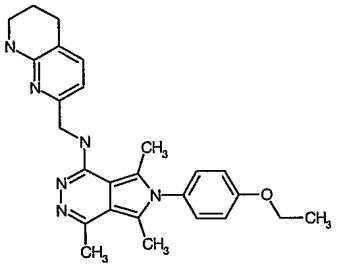
Example 100	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(2-pyridin-2-ylethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		433
Example 101	6-(4-ethoxy-2-methoxyphenyl)-N-isopropyl-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		369
Example 102	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[4-(methylthio)phenyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		450
Example 103	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(4-methylbenzyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		432
Example 104	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(pyridin-3-ylmethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		419

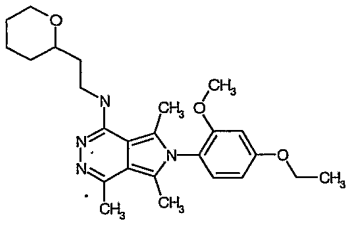
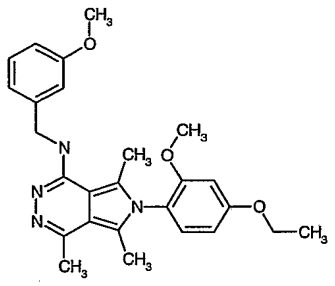
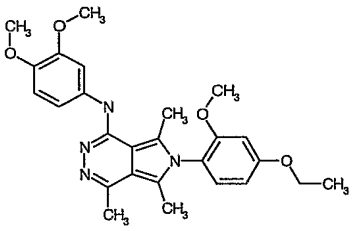
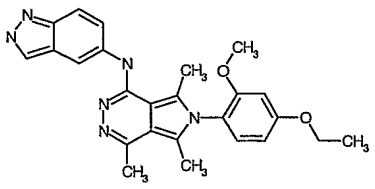
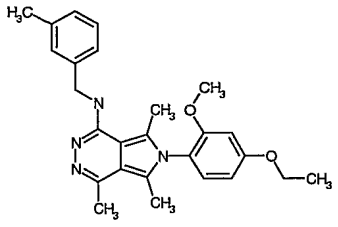
Example 105	6-(4-ethoxy-2-methoxyphenyl)-N-(2,4,5,6,7,8-hexahydrocyclohepta[c]pyrazol-3-ylmethyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		476
Example 106	4-(2-{[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]amino}ethyl)phenol		448
Example 107	N-(3-{[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]amino}phenyl)acetamide		461
Example 108	6-(4-ethoxy-2-methoxyphenyl)-N-(3-fluoro-4-methylphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		436
Example 109	1-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]piperidine-4-carboxamide		439

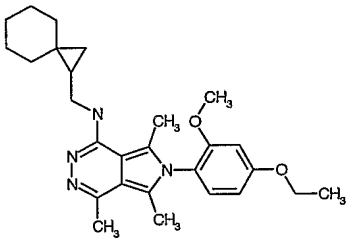
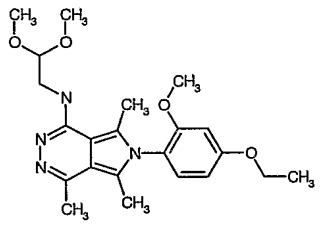
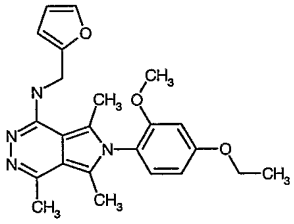
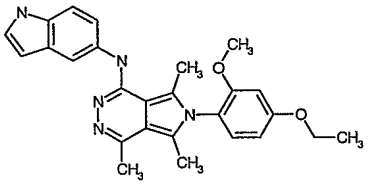
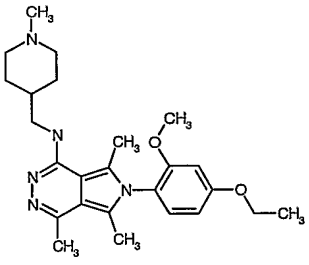
Example 110	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(pyridin-2-ylmethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		419
Example 111	N-butyl-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		384
Example 112	N-(3,4-dimethoxybenzyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		478
Example 113	N-(cyclohexylmethyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		424
Example 114	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(tetrahydrofuran-2-ylmethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		412

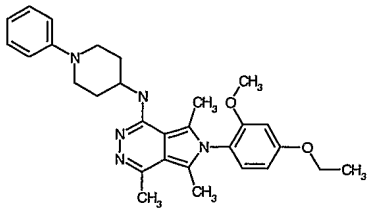
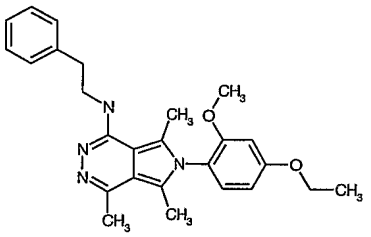
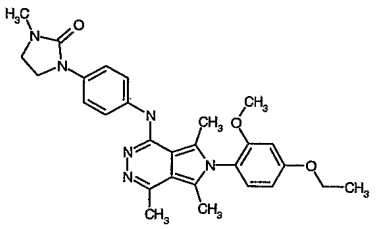
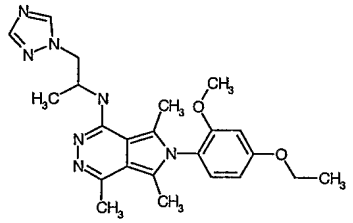
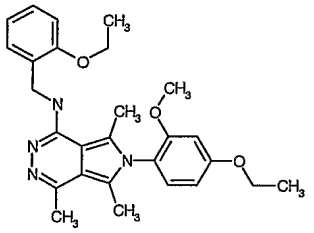
Example 115	N-(2,3-dihydro-1H-inden-1-yl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		444
Example 116	6-(4-ethoxy-2-methoxyphenyl)-N-(4-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		434
Example 117	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(2-methylbenzyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		432
Example 118	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(3-phenylpropyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		446
Example 119	N-(2,3-dihydro-1H-inden-2-ylmethyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		458

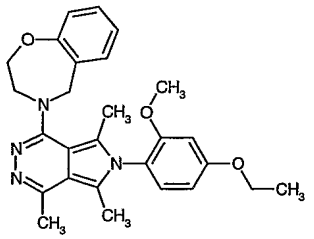
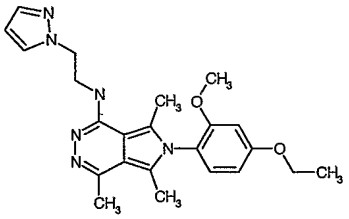
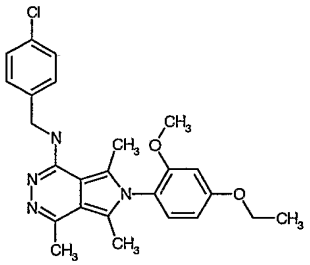
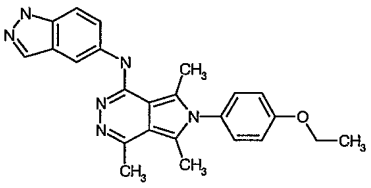
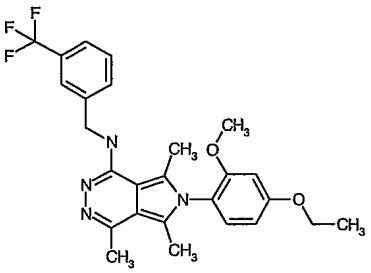
Example 120	6-(4-ethoxy-2-methoxyphenyl)-N-1H-indazol-6-yl-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		444
Example 121	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(1-phenylethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		432
Example 122	6-(4-ethoxyphenyl)-N-1H-indol-5-yl-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		413
Example 123	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(2-methyl-1,3-benzothiazol-6-yl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		475
Example 124	N-cyclopentyl-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		396

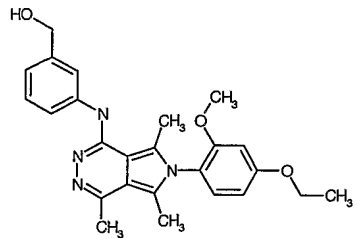
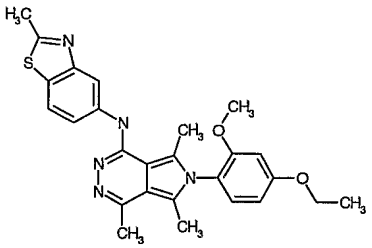
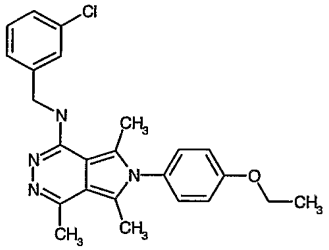
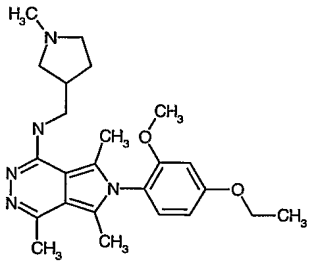
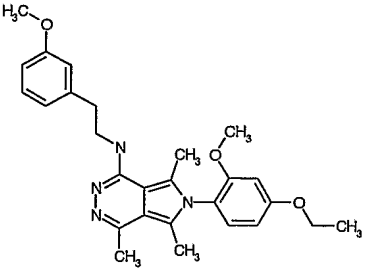
Example 125	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(2-phenylpropyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		446
Example 126	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(4-phenylbutyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		460
Example 127	6-(4-ethoxy-2-methoxyphenyl)-N-[(1-ethyl-1H-pyrazol-4-yl)methyl]-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		436
Example 128	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-ylmethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		444

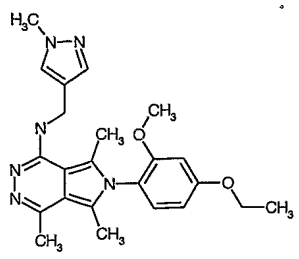
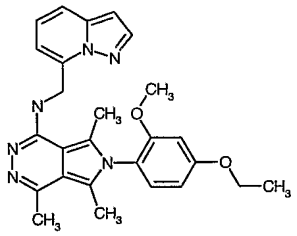
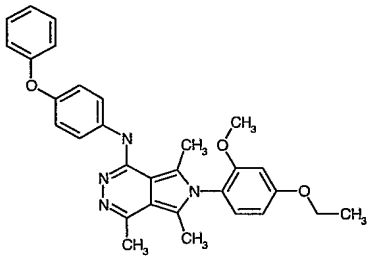
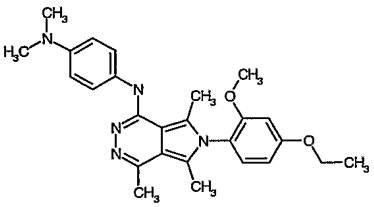
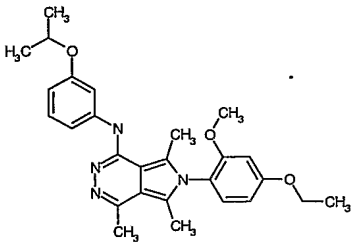
Example 129	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[2-(tetrahydro-2H-pyran-2-yl)ethyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		440
Example 130	6-(4-ethoxy-2-methoxyphenyl)-N-(3-methoxybenzyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		448
Example 131	N-(3,4-dimethoxyphenyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		464
Example 132	6-(4-ethoxy-2-methoxyphenyl)-N-2H-indazol-5-yl-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		444
Example 133	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(3-methylbenzyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		432

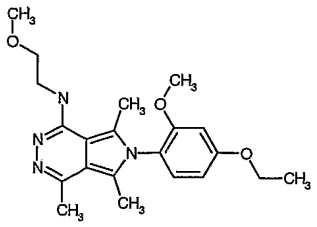
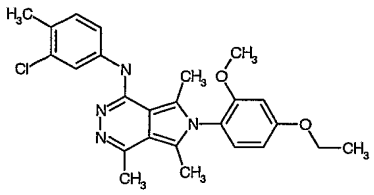
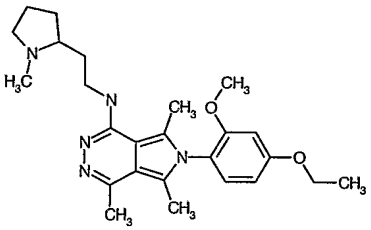
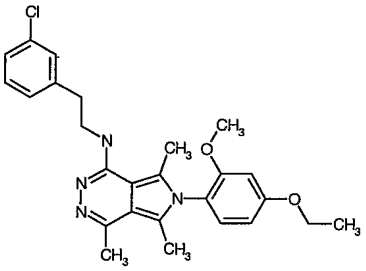
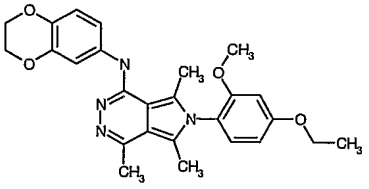
Example 134	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(spiro[2.5]oct-1-ylmethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		450
Example 135	N-(2,2-dimethoxyethyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		416
Example 136	6-(4-ethoxy-2-methoxyphenyl)-N-(2-furylmethyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		407
Example 137	6-(4-ethoxy-2-methoxyphenyl)-N-1H-indol-5-yl-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		443
Example 138	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[(1-methylpiperidin-4-yl)methyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		439

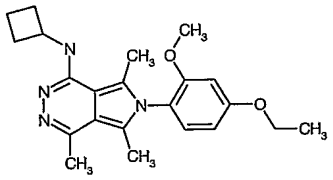
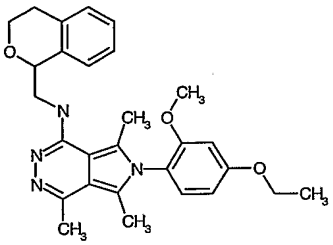
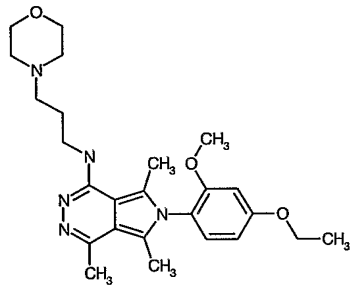
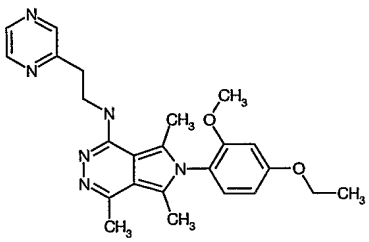
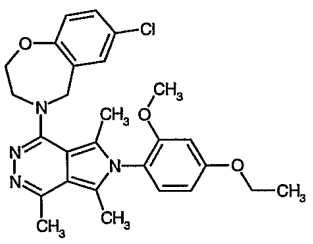
Example 139	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(1-phenylpiperidin-4-yl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		487
Example 140	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(2-phenylethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		432
Example 141	1-(4-{[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]amino}phenyl)-3-methylimidazolidin-2-one		502
Example 142	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[1-methyl-2-(1H-1,2,4-triazol-1-yl)ethyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		437
Example 143	N-(2-ethoxybenzyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		462

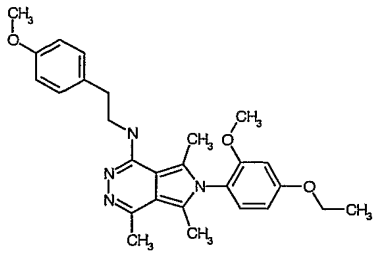
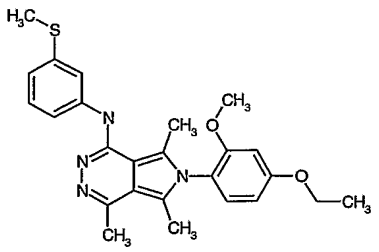
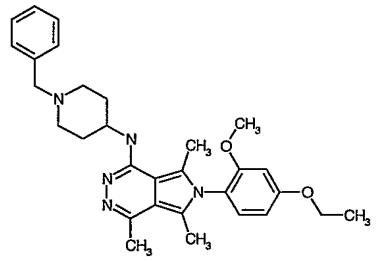
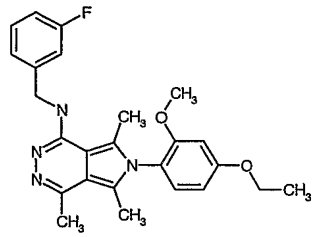
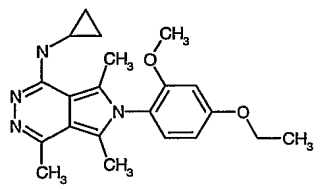
Example 144	4-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-2,3,4,5-tetrahydro-1,4-benzoxazepine		460
Example 145	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[2-(1H-pyrazol-1-yl)ethyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		422
Example 146	N-(4-chlorobenzyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		452
Example 147	6-(4-ethoxyphenyl)-N-1H-indazol-5-yl-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		413
Example 148	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[3-(trifluoromethyl)benzyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		486

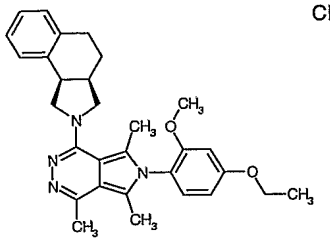
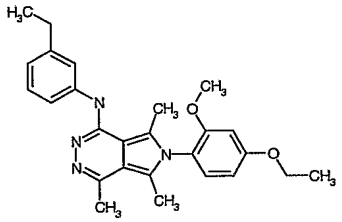
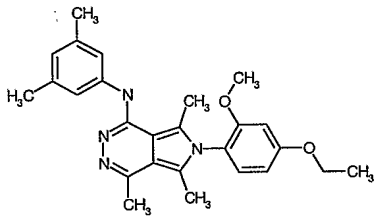
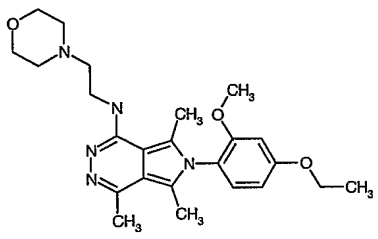
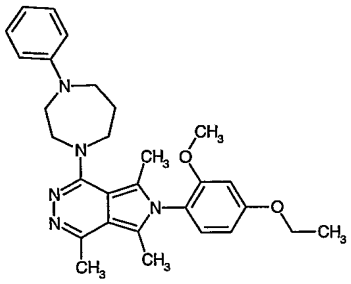
Example 149	(3-{[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]amino}phenyl)methanol		434
Example 150	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(2-methyl-1,3-benzothiazol-5-yl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		475
Example 151	N-(3-chlorobenzyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		422
Example 152	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[(1-methylpyrrolidin-3-yl)methyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		425
Example 153	6-(4-ethoxy-2-methoxyphenyl)-N-[2-(3-methoxyphenyl)ethyl]-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		462

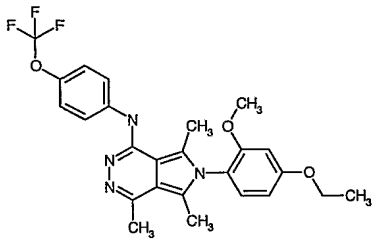
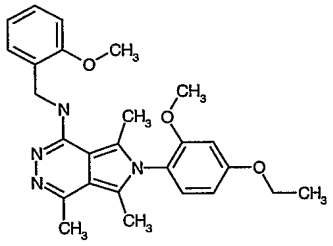
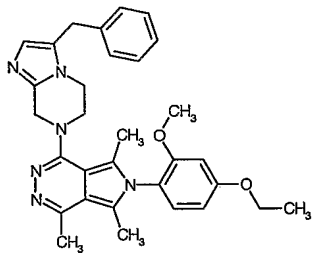
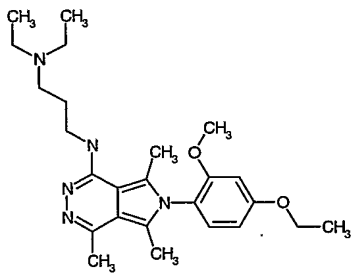
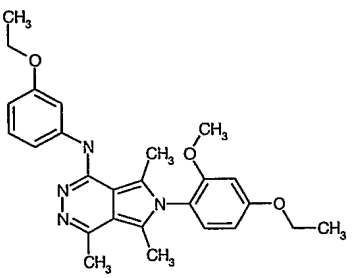
Example 154	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		422
Example 155	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(pyrazolo[1,5-a]pyridin-7-ylmethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		458
Example 156	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(4-phenoxyphenyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		496
Example 157	N'-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-N,N-dimethylbenzene-1,4-diamine		447
Example 158	6-(4-ethoxy-2-methoxyphenyl)-N-(3-isopropoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		462

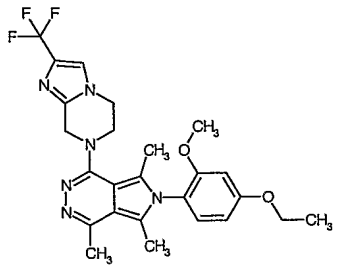
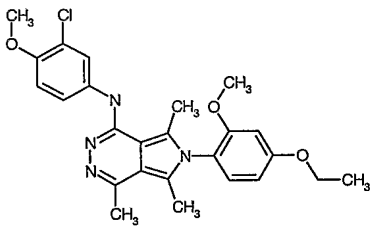
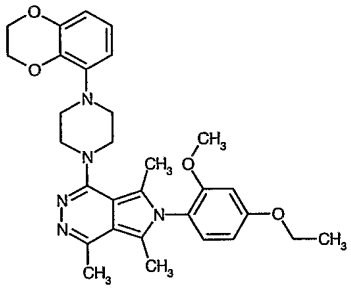
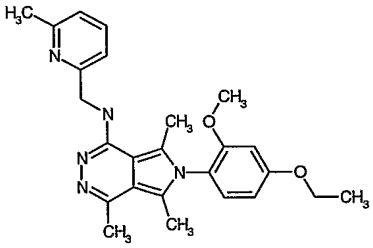
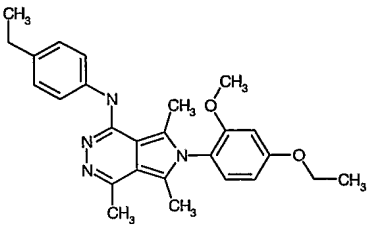
Example 159	6-(4-ethoxy-2-methoxyphenyl)-N-(2-methoxyethyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		385
Example 160	N-(3-chloro-4-methylphenyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		452
Example 161	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[2-(1-methylpyrrolidin-2-yl)ethyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		439
Example 162	N-[2-(3-chlorophenyl)ethyl]-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		466
Example 163	N-(2,3-dihydro-1,4-benzodioxin-6-yl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		462

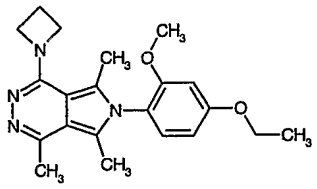
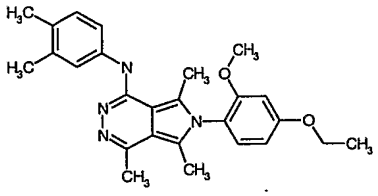
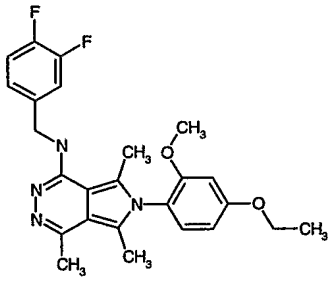
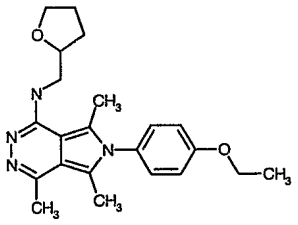
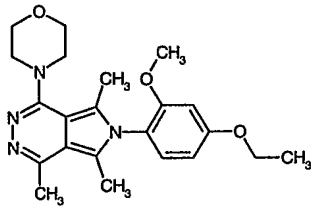
Example 164	N-cyclobutyl-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		381
Example 165	N-(3,4-dihydro-1H-isochromen-1-ylmethyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		474
Example 166	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(3-morpholin-4-ylpropyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		455
Example 167	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(2-pyrazin-2-ylethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		434
Example 168	7-chloro-4-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-2,3,4,5-tetrahydro-1,4-benzoxazepine		494

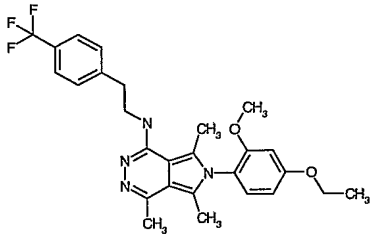
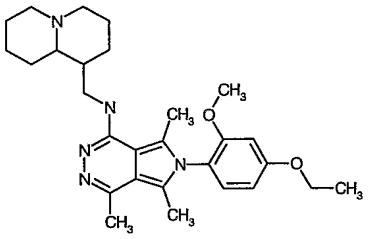
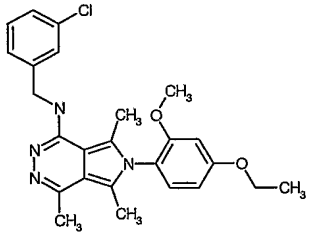
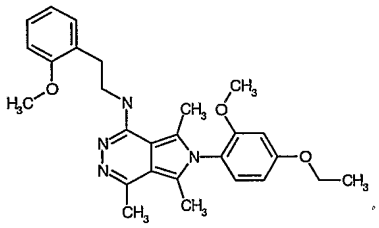
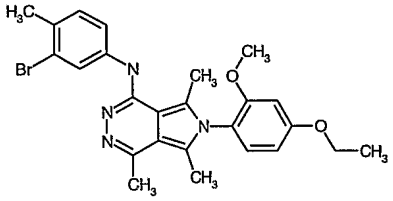
Example 169	6-(4-ethoxy-2-methoxyphenyl)-N-[2-(4-methoxyphenyl)ethyl]-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		462
Example 170	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[3-(methylthio)phenyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		450
Example 171	N-(1-benzylpiperidin-4-yl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		501
Example 172	6-(4-ethoxy-2-methoxyphenyl)-N-(3-fluorobenzyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		436
Example 173	N-cyclopropyl-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		367

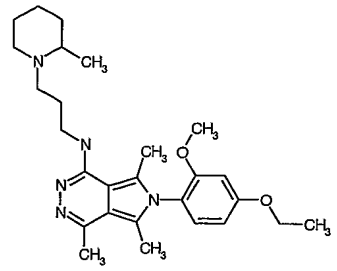
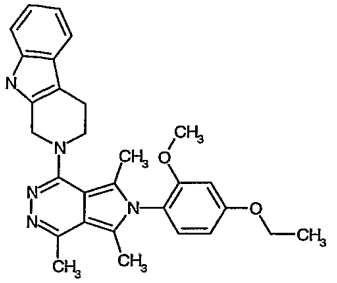
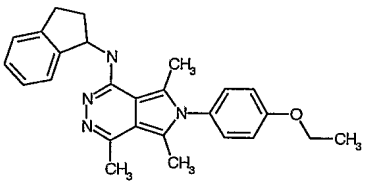
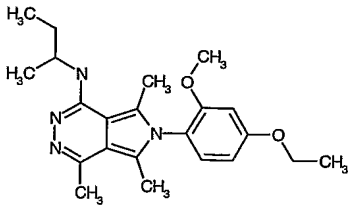
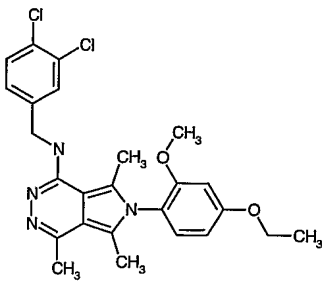
Example 174	(3aR,9bR)-2-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-2,3,3a,4,5,9b-hexahydro-1H-benzo[e]isoindole		Chiral	484
Example 175	6-(4-ethoxy-2-methoxyphenyl)-N-(3-ethylphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine			432
Example 176	N-(3,5-dimethylphenyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine			432
Example 177	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(2-morpholin-4-ylethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine			441
Example 178	6-(4-ethoxy-2-methoxyphenyl)-1,5,7-trimethyl-4-(4-phenyl-1,4-diazepan-1-yl)-6H-pyrrolo[3,4-d]pyridazine			487

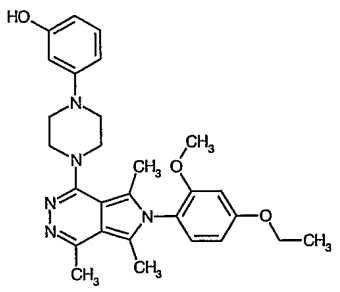
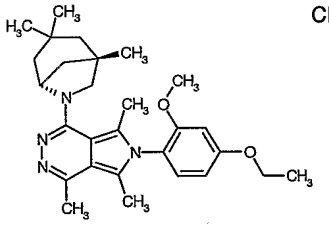
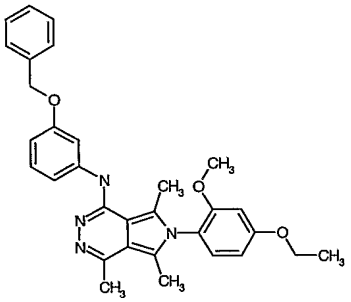
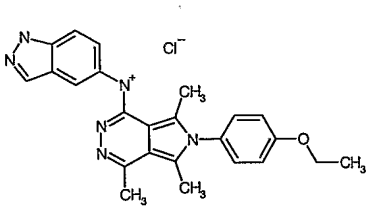
Example 179	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[4-(trifluoromethoxy)phenyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		487
Example 180	6-(4-ethoxy-2-methoxyphenyl)-N-(2-methoxybenzyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		448
Example 181	3-benzyl-7-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine		524
Example 182	N'-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-N,N-diethylpropane-1,3-diamine		441
Example 183	6-(4-ethoxy-2-methoxyphenyl)-N-(3-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		448

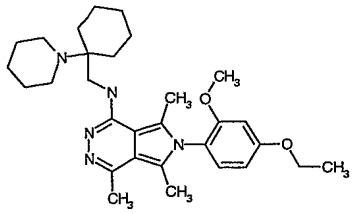
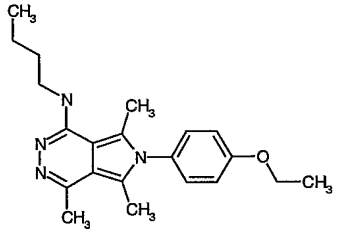
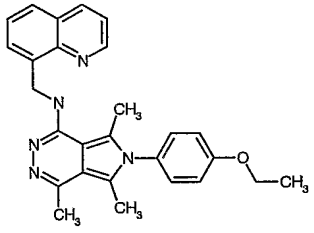
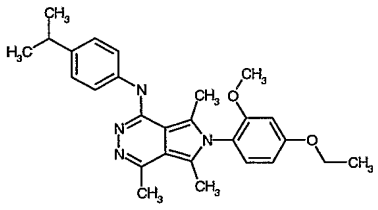
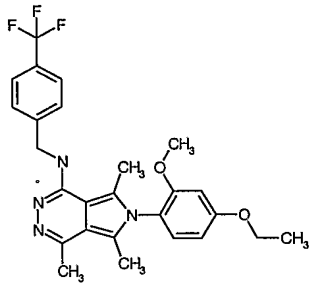
Example 184	7-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-2-(trifluoromethyl)-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine		502
Example 185	N-(3-chloro-4-methoxyphenyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		468
Example 186	1-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazin-1-yl]-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		531
Example 187	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[(6-methylpyridin-2-yl)methyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		433
Example 188	6-(4-ethoxy-2-methoxyphenyl)-N-(4-ethylphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		432

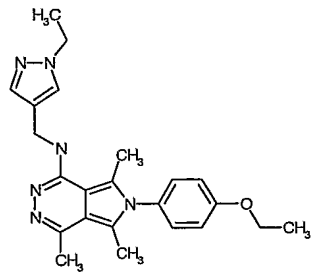
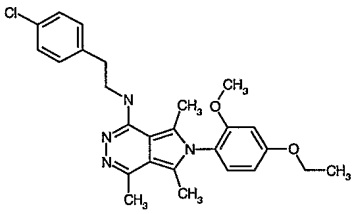
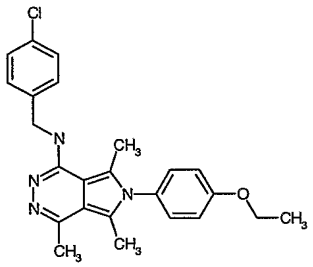
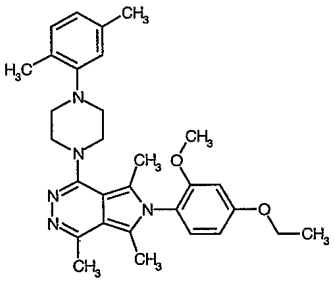
Example 189	1-azetidin-1-yl-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		367
Example 190	N-(3,4-dimethylphenyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		432
Example 191	N-(3,4-difluorobenzyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		454
Example 192	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-(tetrahydrofuran-2-ylmethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		381
Example 193	6-(4-ethoxy-2-methoxyphenyl)-1,5,7-trimethyl-4-morpholin-4-yl-6H-pyrrolo[3,4-d]pyridazine		397

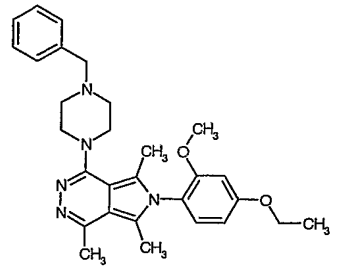
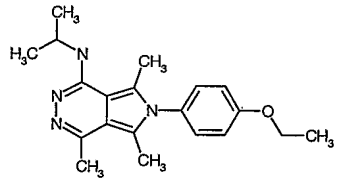
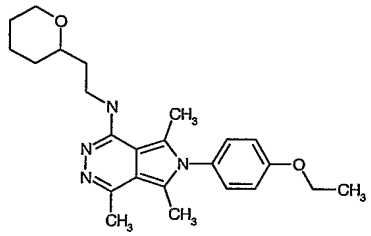
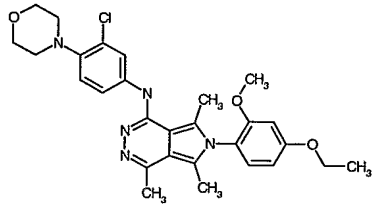
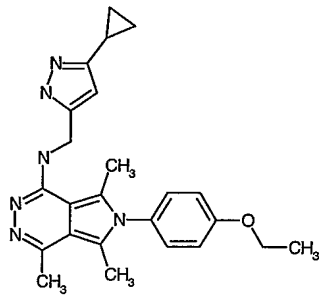
Example 194	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-{2-[4-(trifluoromethyl)phenyl]ethyl}-6H-pyrrolo[3,4-d]pyridazin-1-amine		500
Example 195	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(octahydro-2H-quinolizin-1-ylmethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		479
Example 196	N-(3-chlorobenzyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		452
Example 197	6-(4-ethoxy-2-methoxyphenyl)-N-[2-(2-methoxyphenyl)ethyl]-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		462
Example198	N-(3-bromo-4-methylphenyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		496

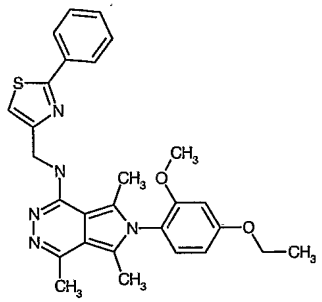
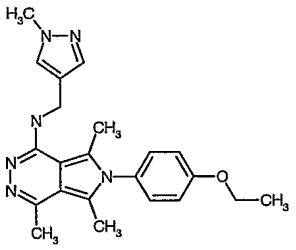
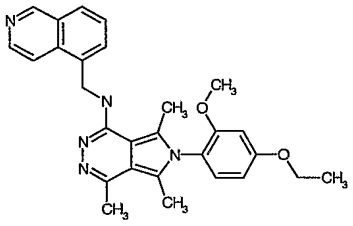
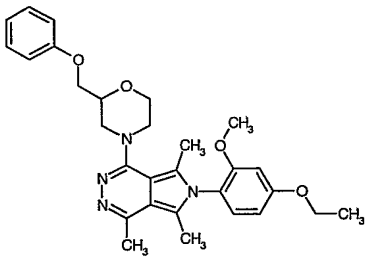
Example 199	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[3-(2-methylpiperidin-1-yl)propyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		467
Example200	2-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-2,3,4,9-tetrahydro-1H-beta-carboline		483
Example 201	N-(2,3-dihydro-1H-inden-1-yl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		414
Example 202	N-(sec-butyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		384
Example 203	N-(3,4-dichlorobenzyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		486

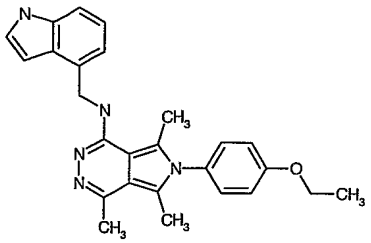
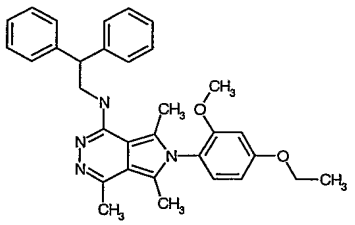
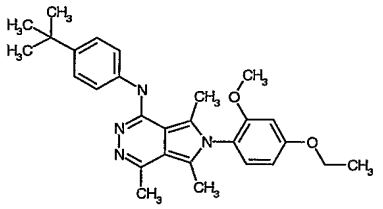
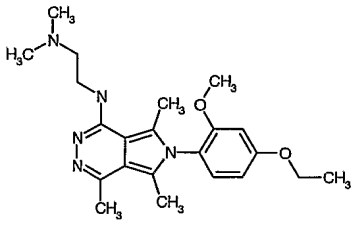
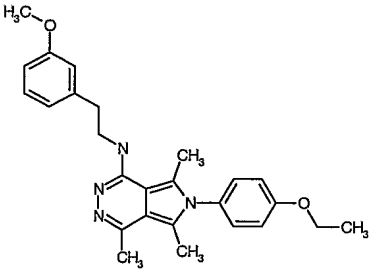
Example 204	3-{4-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]piperazin-1-yl}phenol			489
Example 205	6-(4-ethoxy-2-methoxyphenyl)-1,5,7-trimethyl-4-[(1S,5R)-1,3,3-trimethyl-6-azabicyclo[3.2.1]oct-6-yl]-6H-pyrrolo[3,4-d]pyridazine		Chiral	464
Example 206	N-[3-(benzyloxy)phenyl]-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine			510
Example 207	6-(4-ethoxyphenyl)-N-1H-indazol-5-yl-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-aminium chloride			450

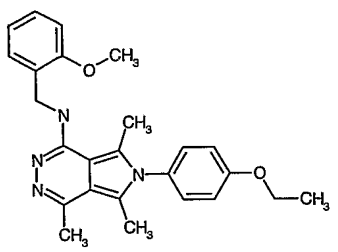
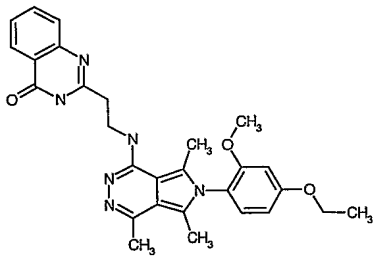
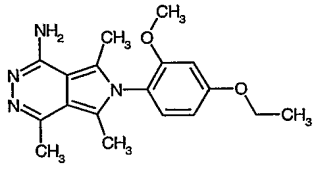
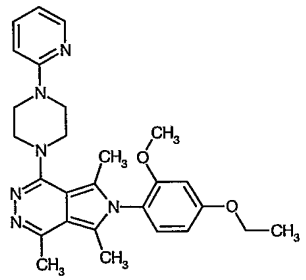
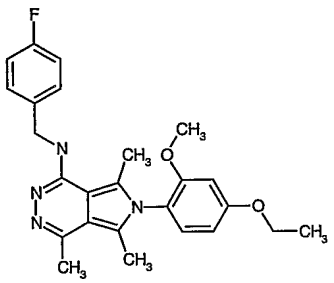
Example 208	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[(1-piperidin-1-ylcyclohexyl)methyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		507
Example 209	N-butyl-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		353
Example 210	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-(quinolin-8-ylmethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		439
Example 211	6-(4-ethoxy-2-methoxyphenyl)-N-(4-isopropylphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		446
Example 212	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[4-(trifluoromethyl)benzyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		486

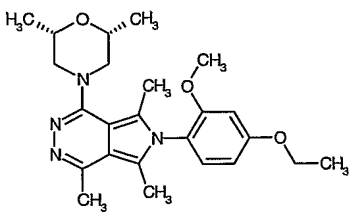
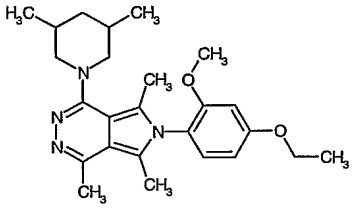
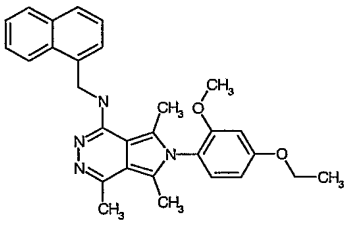
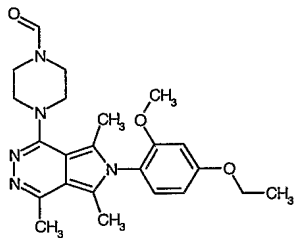
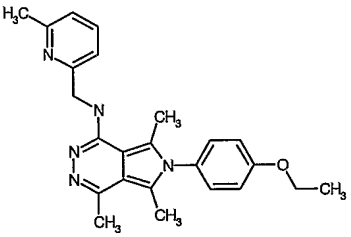
Example 213	6-(4-ethoxyphenyl)-N-[(1-ethyl-1H-pyrazol-4-yl)methyl]-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		406
Example 214	N-[2-(4-chlorophenyl)ethyl]-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		466
Example 215	N-(4-chlorobenzyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		422
Example 216	1-[4-(2,5-dimethylphenyl)piperazin-1-yl]-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		501

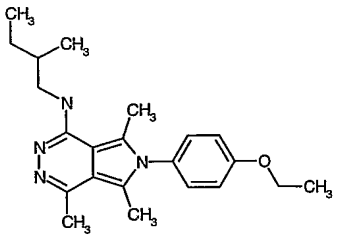
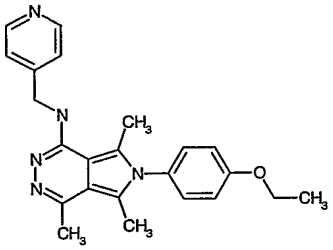
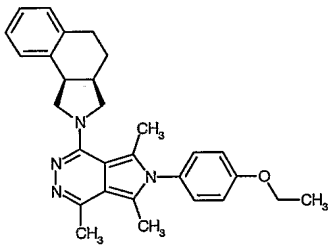
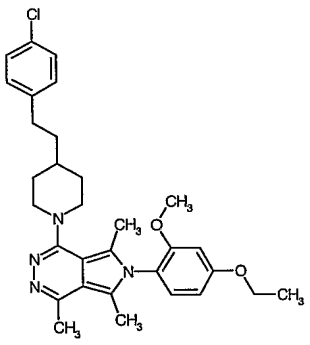
Example 217	1-(4-benzylpiperazin-1-yl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		487
Example 218	6-(4-ethoxyphenyl)-N-isopropyl-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		339
Example 219	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-[2-(tetrahydro-2H-pyran-2-yl)ethyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		410
Example 220	N-(3-chloro-4-morpholin-4-ylphenyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		523
Example 221	N-[(3-cyclopropyl-1H-pyrazol-5-yl)methyl]-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		418

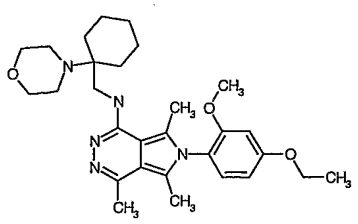
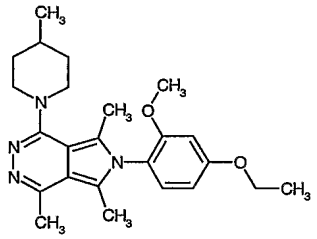
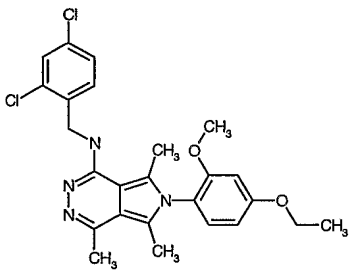
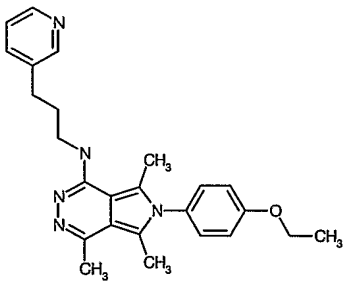
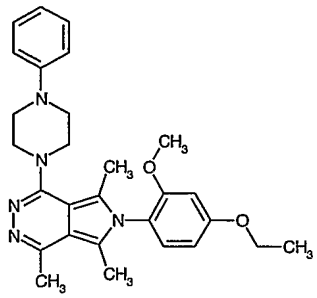
Example 222	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[(2-phenyl-1,3-thiazol-4-yl)methyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		501
Example 223	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		391
Example 224	6-(4-ethoxy-2-methoxyphenyl)-N-(isoquinolin-5-ylmethyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		469
Example 225	6-(4-ethoxy-2-methoxyphenyl)-1,5,7-trimethyl-4-[2-(phenoxymethyl)morpholin-4-yl]-6H-pyrrolo[3,4-d]pyridazine		504

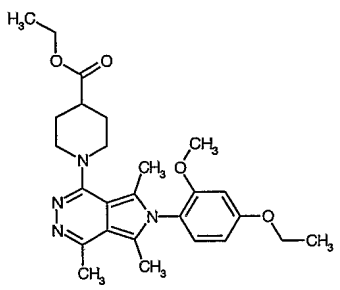
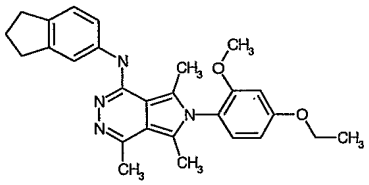
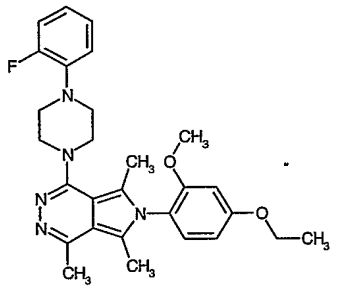
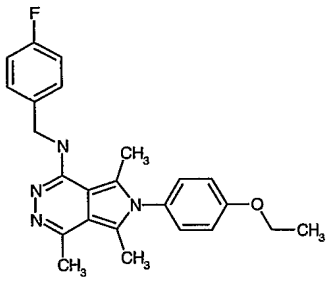
Example 226	6-(4-ethoxyphenyl)-N-(1H-indol-4-ylmethyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		427
Example 227	N-(2,2-diphenylethyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		508
Example 228	N-(4-tert-butylphenyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		460
Example 229	N'-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-N,N-dimethylethane-1,2-diamine		399
Example 230	6-(4-ethoxyphenyl)-N-[2-(3-methoxyphenyl)ethyl]-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		432

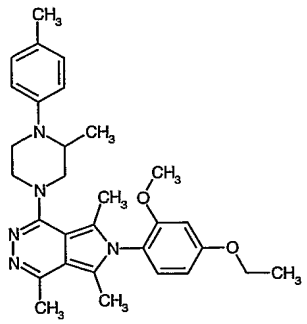
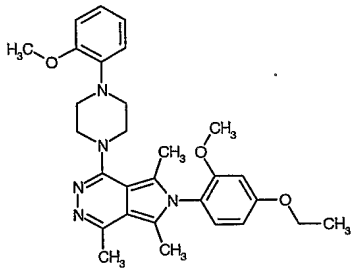
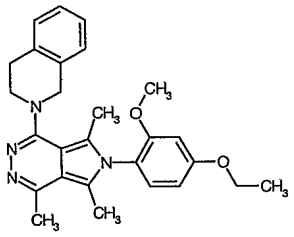
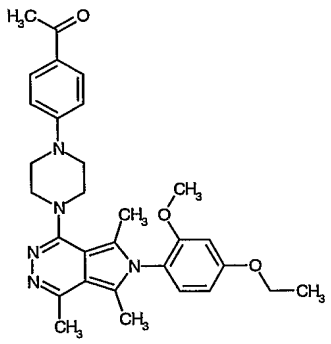
Example 231	6-(4-ethoxyphenyl)-N-(2-methoxybenzyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		418
Example 232	2-(2-{[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]amino}ethyl)quinazolin-4(3H)-one		500
Example 233	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		327
Example 234	6-(4-ethoxy-2-methoxyphenyl)-1,5,7-trimethyl-4-(4-pyridin-2-ylpiperazin-1-yl)-6H-pyrrolo[3,4-d]pyridazine		474
Example 235	6-(4-ethoxy-2-methoxyphenyl)-N-(4-fluorobenzyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		436

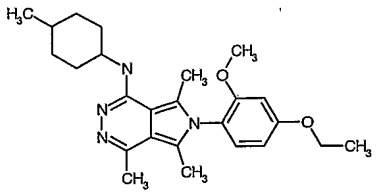
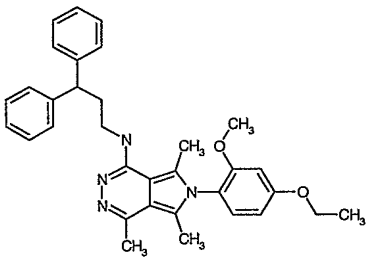
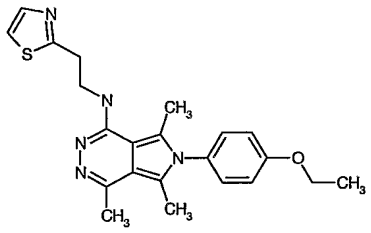
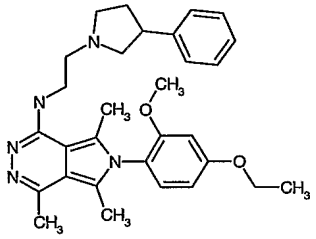
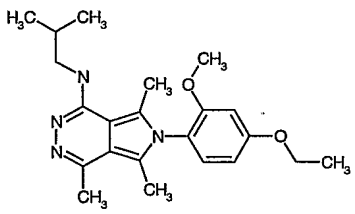
Example 236	1-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		426
Example 237	1-(3,5-dimethylpiperidin-1-yl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		424
Example 238	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(1-naphthylmethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		468
Example 239	4-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]piperazine-1-carbaldehyde		425
Example 240	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-[(6-methylpyridin-2-yl)methyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		403

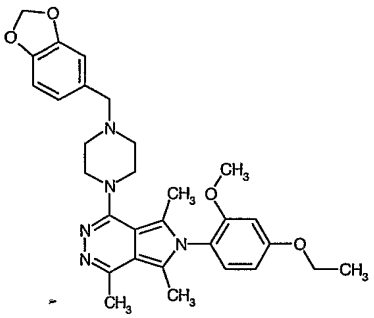
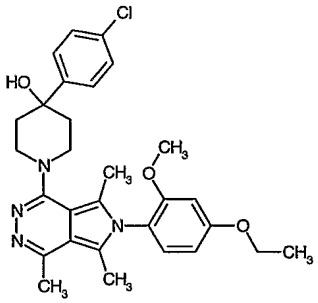
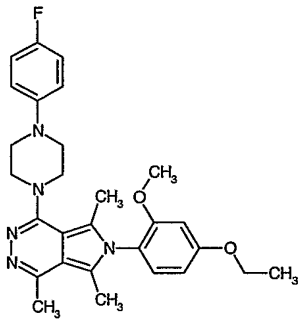
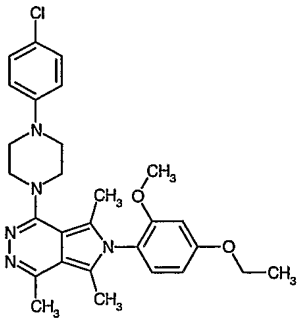
Example 241	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-(2-methylbutyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		368
Example 242	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-(pyridin-4-ylmethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		388
Example 243	(3aR,9bR)-2-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-2,3,3a,4,5,9b-hexahydro-1H-benzo[e]isoindole		454
Example 244	1-{4-[2-(4-chlorophenyl)ethyl]piperidin-1-yl}-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		534

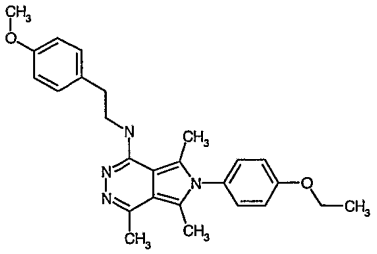
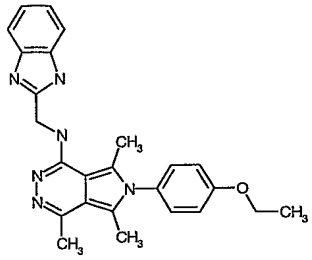
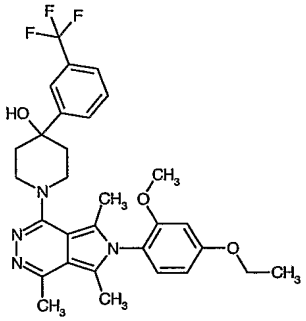
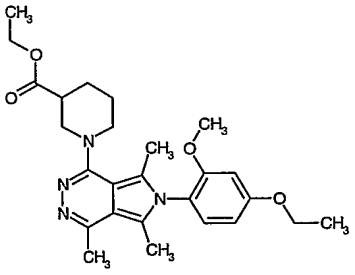
Example 245	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[(1-morpholin-4-ylcyclohexyl)methyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		509
Example 246	6-(4-ethoxy-2-methoxyphenyl)-1,5,7-trimethyl-4-(4-methylpiperidin-1-yl)-6H-pyrrolo[3,4-d]pyridazine		410
Example 247	N-(2,4-dichlorobenzyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		486
Example 248	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-(3-pyridin-3-ylpropyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		417
Example 249	6-(4-ethoxy-2-methoxyphenyl)-1,5,7-trimethyl-4-(4-phenylpiperazin-1-yl)-6H-pyrrolo[3,4-d]pyridazine		473

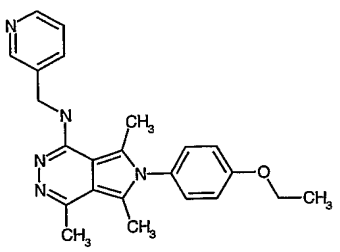
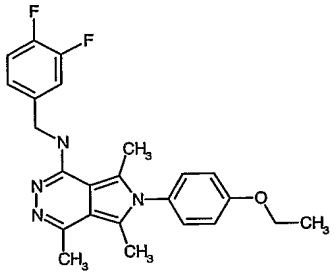
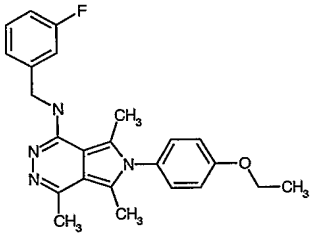
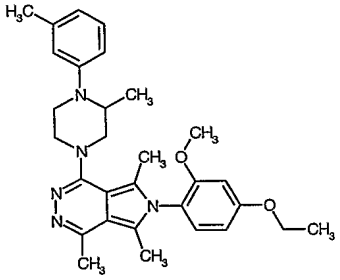
Example 250	ethyl 1-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]piperidine-4-carboxylate		468
Example 251	N-(2,3-dihydro-1H-inden-5-yl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		444
Example 252	6-(4-ethoxy-2-methoxyphenyl)-1-[4-(2-fluorophenyl)piperazin-1-yl]-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		491
Example 253	6-(4-ethoxyphenyl)-N-(4-fluorobenzyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		405

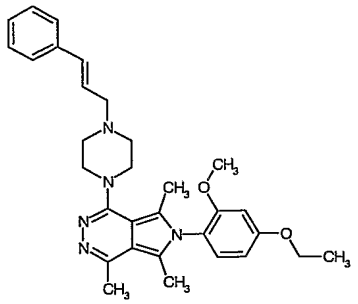
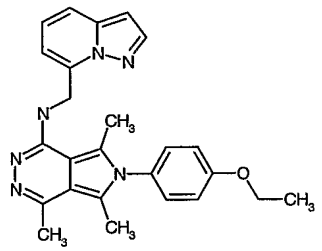
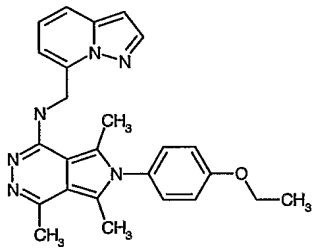
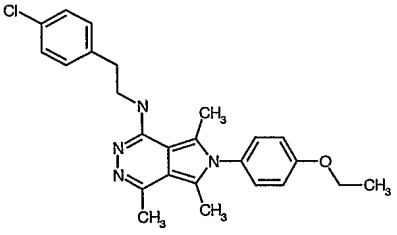
Example 254	6-(4-ethoxy-2-methoxyphenyl)-1,5,7-trimethyl-4-[3-methyl-4-(4-methylphenyl)piperazin-1-yl]-6H-pyrrolo[3,4-d]pyridazine		501
Example 255	6-(4-ethoxy-2-methoxyphenyl)-1-[4-(2-methoxyphenyl)piperazin-1-yl]-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		503
Example 256	2-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-1,2,3,4-tetrahydroisoquinoline		444
Example 257	1-(4-{4-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]piperazin-1-yl}phenyl)ethanone		515

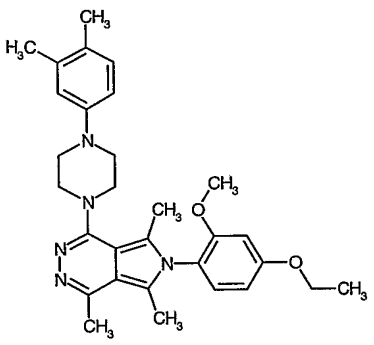
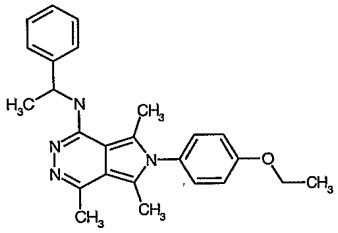
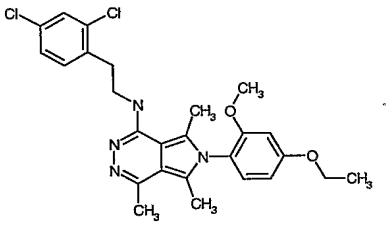
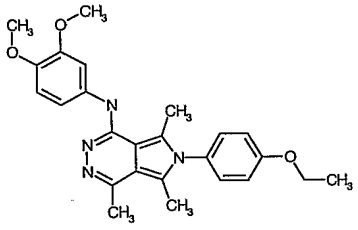
Example 258	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(4-methylcyclohexyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		424
Example 259	N-(3,3-diphenylpropyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		522
Example 260	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-[2-(1,3-thiazol-2-yl)ethyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		409
Example 261	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[2-(3-phenylpyrrolidin-1-yl)ethyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		501
Example 262	6-(4-ethoxy-2-methoxyphenyl)-N-isobutyl-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		384

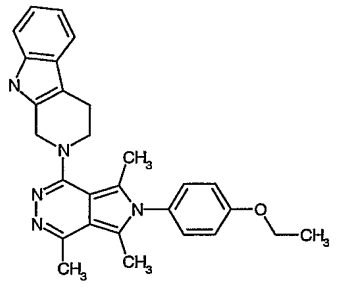
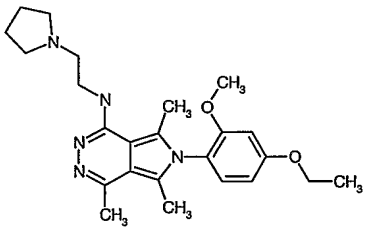
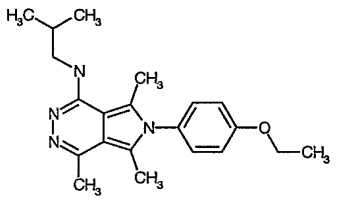
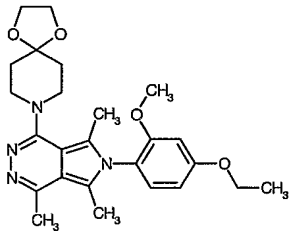
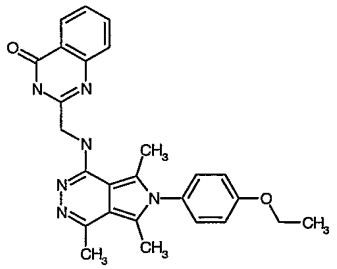
Example 263	1-[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		531
Example 264	4-(4-chlorophenyl)-1-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]piperidin-4-ol		522
Example 265	6-(4-ethoxy-2-methoxyphenyl)-1-[4-(4-fluorophenyl)piperazin-1-yl]-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		491
Example 266	1-[4-(4-chlorophenyl)piperazin-1-yl]-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		507

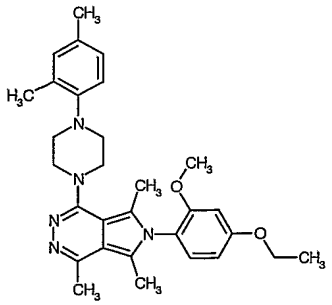
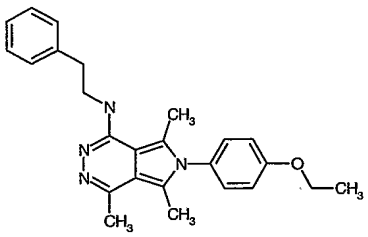
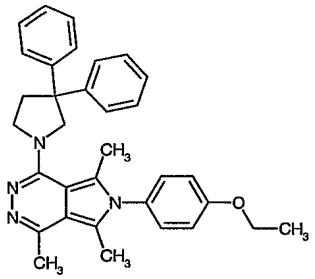
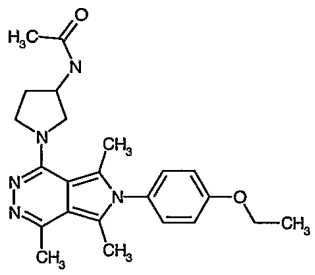
Example 267	6-(4-ethoxyphenyl)-N-[2-(4-methoxyphenyl)ethyl]-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		432
Example 268	N-(1H-benzimidazol-2-ylmethyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		428
Example 269	1-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-4-[3-(trifluoromethyl)phenyl]piperidin-4-ol		556
Example 270	ethyl 1-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]piperidine-3-carboxylate		468

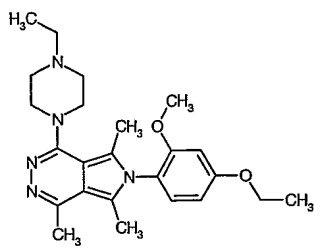
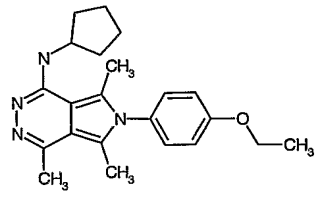
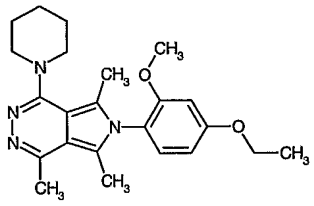
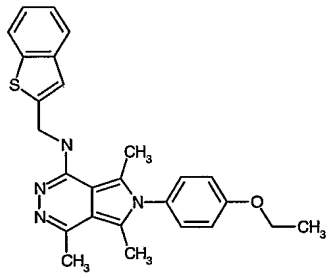
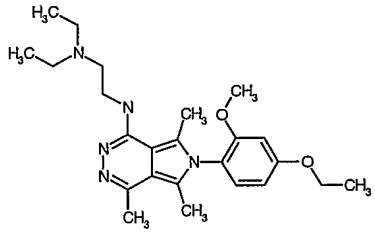
Example 271	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-(pyridin-3-ylmethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		388
Example 272	N-(3,4-difluorobenzyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		423
Example 273	6-(4-ethoxyphenyl)-N-(3-fluorobenzyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		405
Example 274	6-(4-ethoxy-2-methoxyphenyl)-1,5,7-trimethyl-4-[3-methyl-4-(3-methylphenyl)piperazin-1-yl]-6H-pyrrolo[3,4-d]pyridazine		501

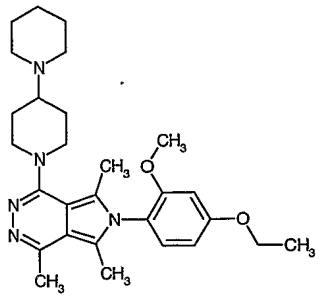
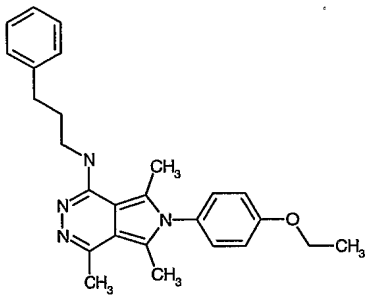
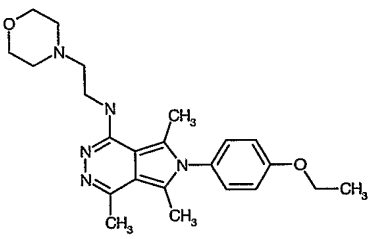
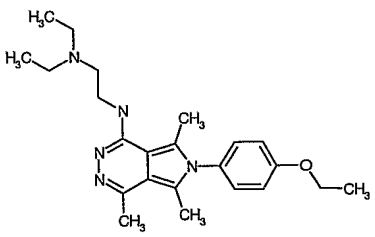
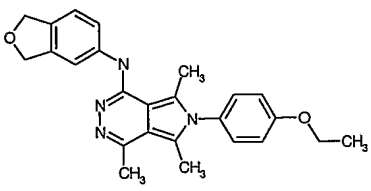
Example 275	6-(4-ethoxy-2-methoxyphenyl)-1,5,7-trimethyl-4-{4-[(2E)-3-phenylprop-2-en-1-yl]piperazin-1-yl}-6H-pyrrolo[3,4-d]pyridazine		513
Example 276	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-(pyrazolo[1,5-a]pyridin-7-ylmethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		428
Example 277	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-(pyrazolo[1,5-a]pyridin-7-ylmethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		428
Example 278	N-[2-(4-chlorophenyl)ethyl]-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		436

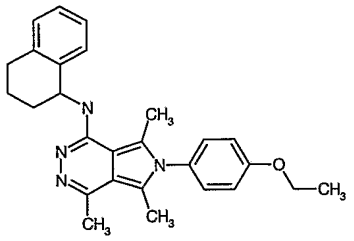
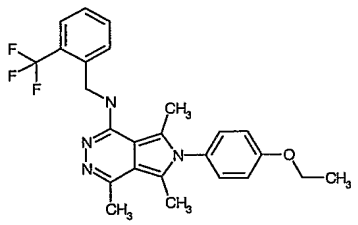
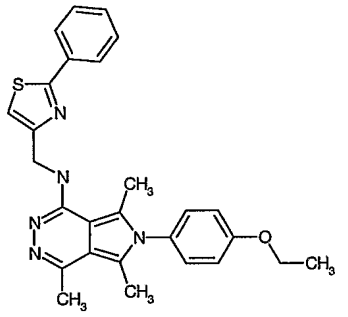
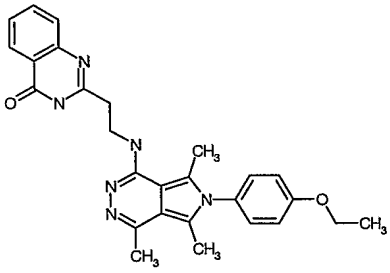
Example 279	1-[4-(3,4-dimethylphenyl)piperazin-1-yl]-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		501
Example 280	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-(1-phenylethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		402
Example 281	N-[2-(2,4-dichlorophenyl)ethyl]-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		500
Example 282	N-(3,4-dimethoxyphenyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		434

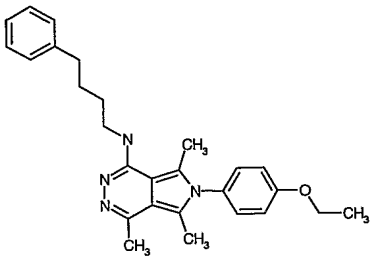
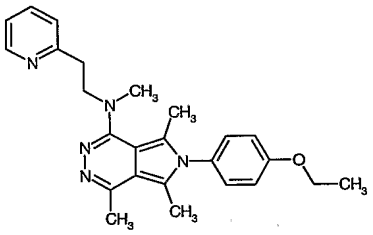
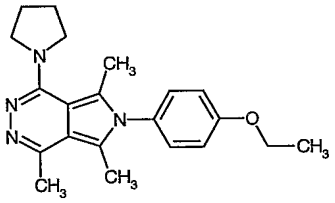
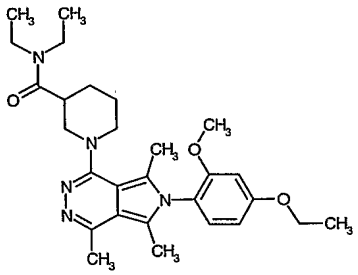
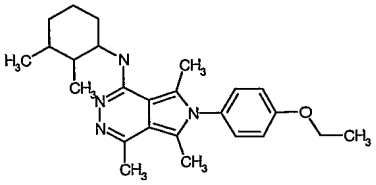
Example 283	2-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-2,3,4,9-tetrahydro-1H-beta-carboline		453
Example 284	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-(2-pyrrolidin-1-ylethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		425
Example 285	6-(4-ethoxyphenyl)-N-isobutyl-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		353
Example 286	8-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-1,4-dioxa-8-azaspiro[4.5]decane		454
Example 287	2-({[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]amino}methyl)quinazolin-4(3H)-one		456

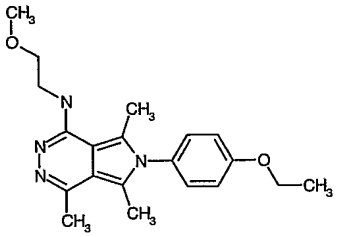
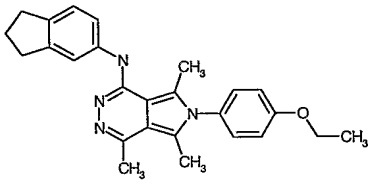
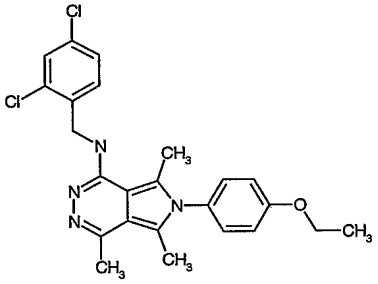
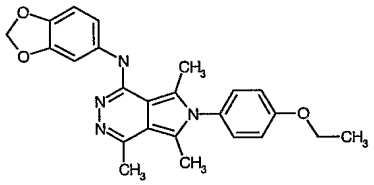
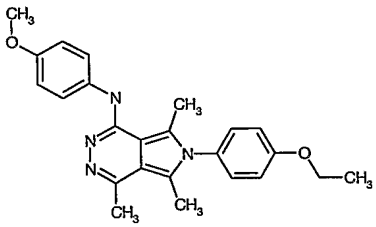
Example 288	1-[4-(2,4-dimethylphenyl)piperazin-1-yl]-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		501
Example 289	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-(2-phenylethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		402
Example 290	1-(3,3-diphenylpyrrolidin-1-yl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		504
Example 291	N-{1-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]pyrrolidin-3-yl}acetamide		409

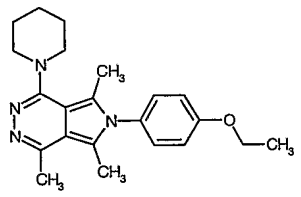
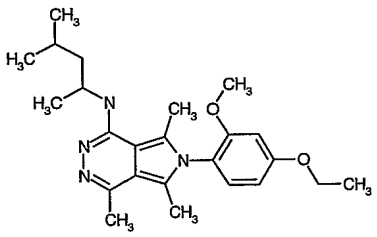
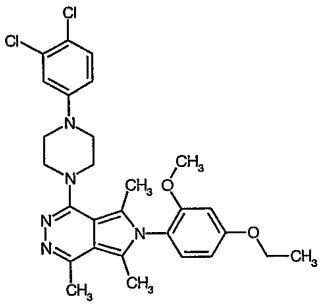
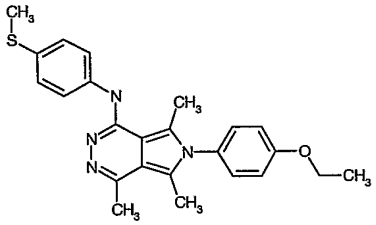
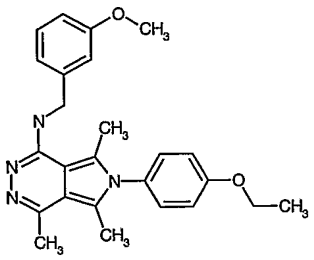
Example 292	6-(4-ethoxy-2-methoxyphenyl)-1-(4-ethylpiperazin-1-yl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		425
Example 293	N-cyclopentyl-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		365
Example 294	6-(4-ethoxy-2-methoxyphenyl)-1,5,7-trimethyl-4-piperidin-1-yl-6H-pyrrolo[3,4-d]pyridazine		396
Example 295	N-(1-benzothien-2-ylmethyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		444
Example 296	N'-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-N,N-diethylethane-1,2-diamine		427

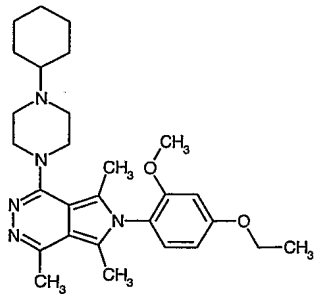
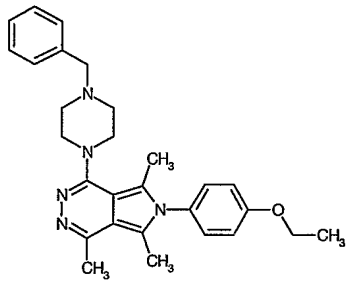
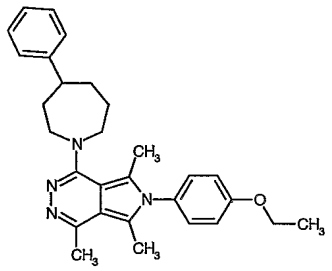
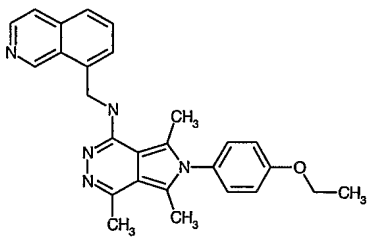
Example 297	1'-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-1,4'-bipiperidine		479
Example 298	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-(3-phenylpropyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		416
Example 299	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-(2-morpholin-4-ylethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		411
Example 300	N'-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-N,N-diethylethane-1,2-diamine		397
Example 301	N-(1,3-dihydro-2-benzofuran-5-yl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		416

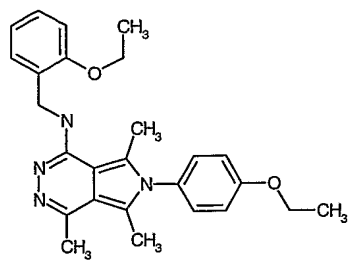
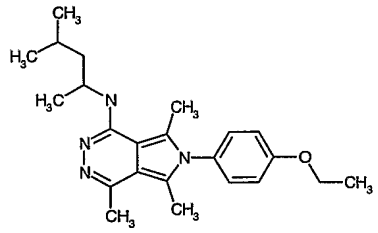
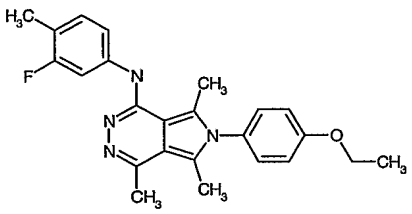
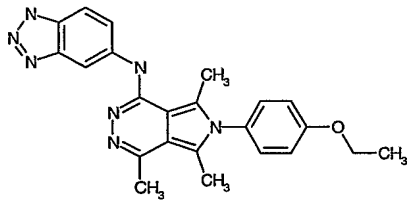
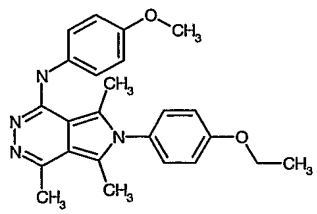
Example 302	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-(1,2,3,4-tetrahydronaphthalen-1-yl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		428
Example 303	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-[2-(trifluoromethyl)benzyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		455
Example 304	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-[(2-phenyl-1,3-thiazol-4-yl)methyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		471
Example 305	2-(2-{[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]amino}ethyl)quinazolin-4(3H)-one		470

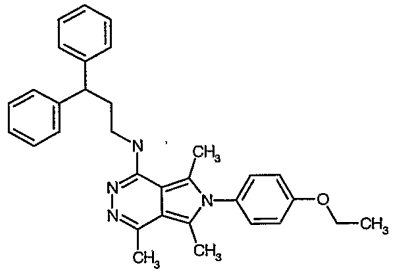
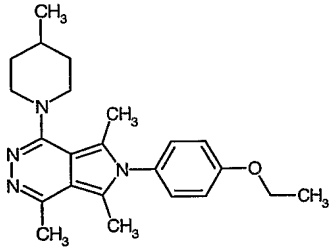
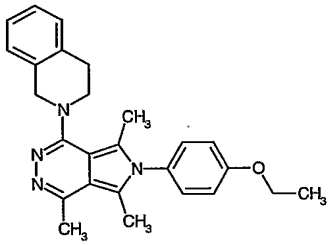
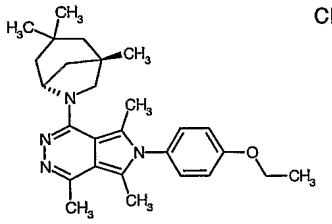
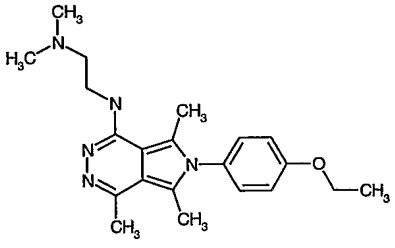
Example 306	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-(4-phenylbutyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		430
Example 307	6-(4-ethoxyphenyl)-N,4,5,7-tetramethyl-N-(2-pyridin-2-ylethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		417
Example 308	6-(4-ethoxyphenyl)-1,5,7-trimethyl-4-pyrrolidin-1-yl-6H-pyrrolo[3,4-d]pyridazine		351
Example 309	1-[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-N,N-diethylpiperidine-3-carboxamide		495
Example 310	N-(2,3-dimethylcyclohexyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		408

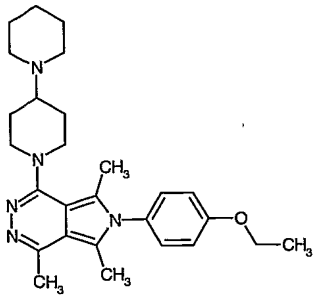
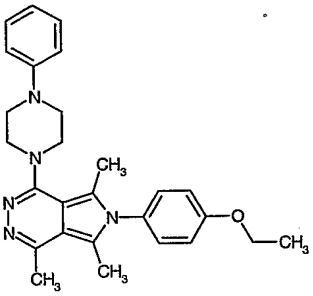
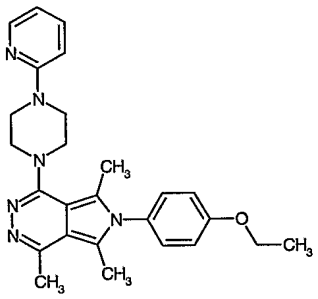
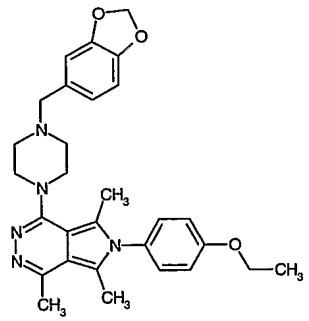
Example 311	6-(4-ethoxyphenyl)-N-(2-methoxyethyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		355
Example 312	N-(2,3-dihydro-1H-inden-5-yl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		414
Example 313	N-(2,4-dichlorobenzyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		456
Example 314	N-1,3-benzodioxol-5-yl-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		417
Example 315	6-(4-ethoxyphenyl)-N-(4-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		404

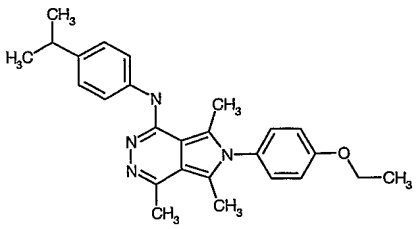
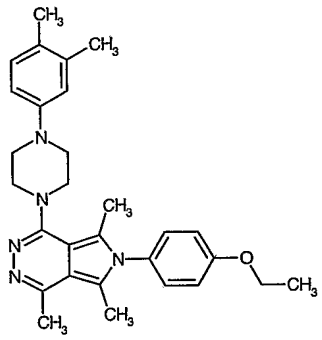
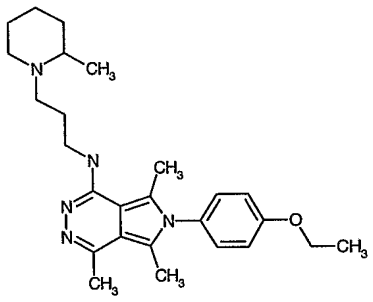
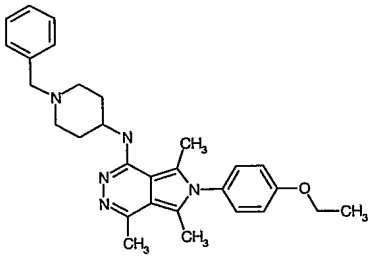
Example 316	6-(4-ethoxyphenyl)-1,5,7-trimethyl-4-piperidin-1-yl-6H-pyrrolo[3,4-d]pyridazine		365
Example 317	N-(1,3-dimethylbutyl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		412
Example 318	1-[4-(3,4-dichlorophenyl)piperazin-1-yl]-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		541
Example 319	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-[4-(methylthio)phenyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		420
Example 320	6-(4-ethoxyphenyl)-N-(3-methoxybenzyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		418

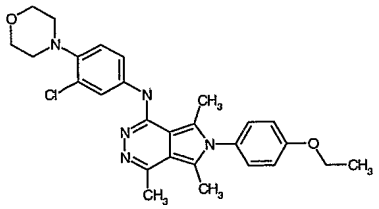
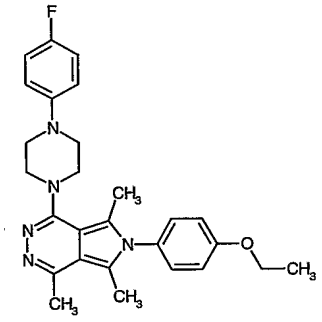
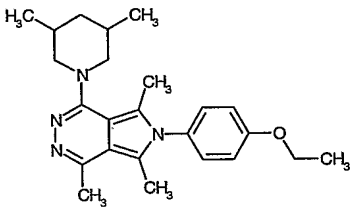
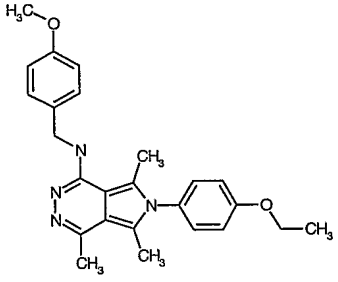
Example 321	1-(4-cyclohexylpiperazin-1-yl)-6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		479
Example 322	1-(4-benzylpiperazin-1-yl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		457
Example 323	6-(4-ethoxyphenyl)-1,5,7-trimethyl-4-(4-phenylazepan-1-yl)-6H-pyrrolo[3,4-d]pyridazine		456
Example 324	6-(4-ethoxyphenyl)-N-(isoquinolin-8-ylmethyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		439

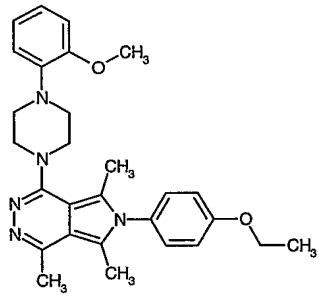
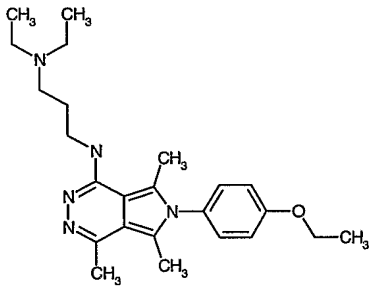
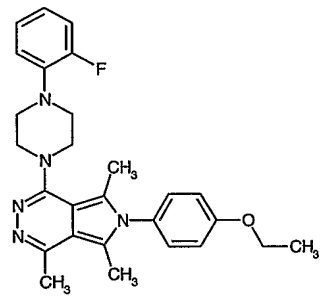
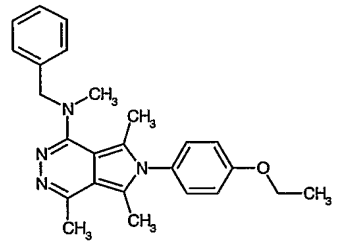
Example 325	N-(2-ethoxybenzyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		432
Example 326	N-(1,3-dimethylbutyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		382
Example 327	6-(4-ethoxyphenyl)-N-(3-fluoro-4-methylphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		405
Example 328	N-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-1H-1,2,3-benzotriazol-5-amine		414
Example 329	6-(4-ethoxyphenyl)-N-(4-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		404

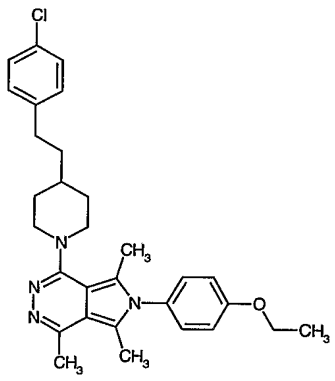
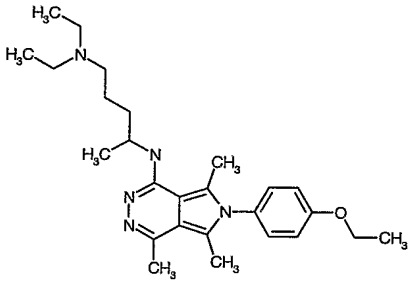
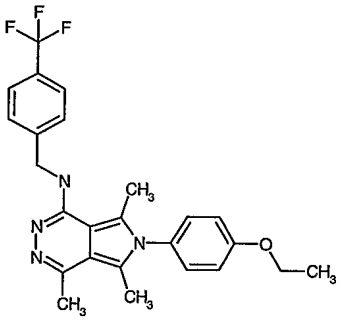
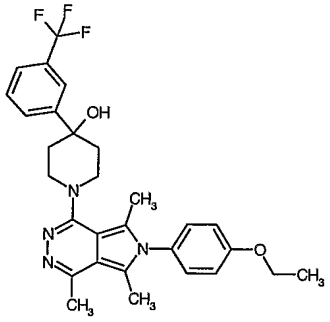
Example 330	N-(3,3-diphenylpropyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		492
Example 331	6-(4-ethoxyphenyl)-1,5,7-trimethyl-4-(4-methylpiperidin-1-yl)-6H-pyrrolo[3,4-d]pyridazine		380
Example 332	2-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-1,2,3,4-tetrahydroisoquinoline		414
Example 333	N'-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-N,N-dimethylethane-1,2-diamine	 Chiral	368
Example 334	6-(4-ethoxyphenyl)-1,5,7-trimethyl-4-[(1S,5R)-1,3,3-trimethyl-6-azabicyclo[3.2.1]oct-6-yl]-6H-pyrrolo[3,4-d]pyridazine		434

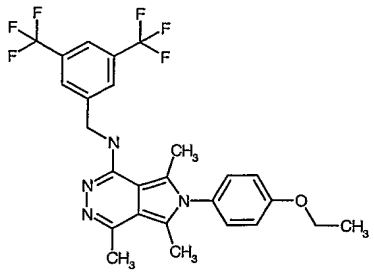
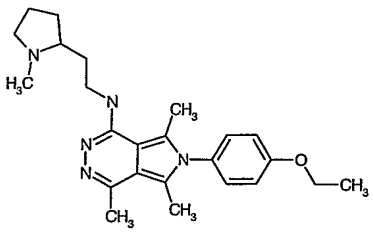
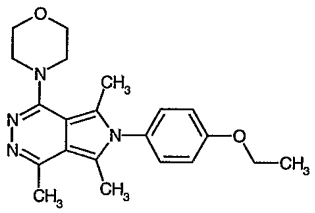
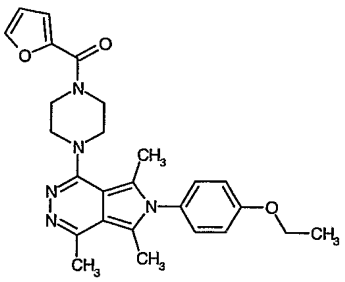
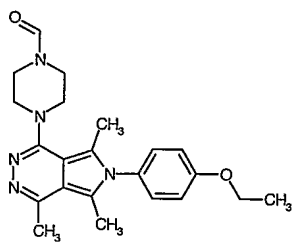
Example 335	1'-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-1,4'-bipiperidine		449
Example 336	6-(4-ethoxyphenyl)-1,5,7-trimethyl-4-(4-phenylpiperazin-1-yl)-6H-pyrrolo[3,4-d]pyridazine		443
Example 337	6-(4-ethoxyphenyl)-1,5,7-trimethyl-4-(4-pyridin-2-ylpiperazin-1-yl)-6H-pyrrolo[3,4-d]pyridazine		444
Example 338	1-[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		501

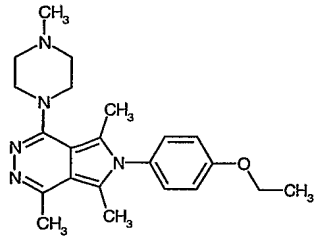
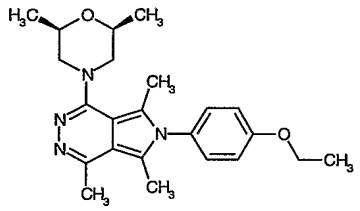
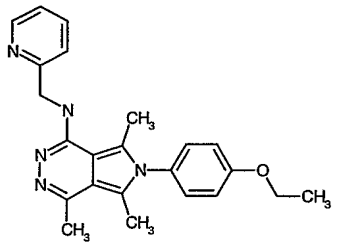
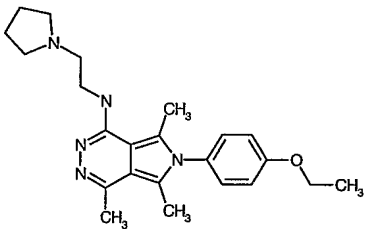
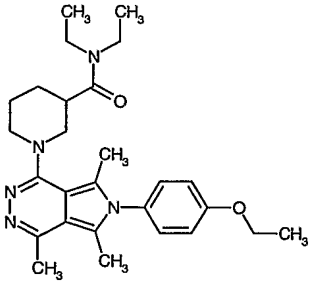
Example 339	6-(4-ethoxyphenyl)-N-(4-isopropylphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		416
Example 340	1-[4-(3,4-dimethylphenyl)piperazin-1-yl]-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		471
Example 341	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-[3-(2-methylpiperidin-1-yl)propyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		437
Example 342	N-(1-benzylpiperidin-4-yl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		471

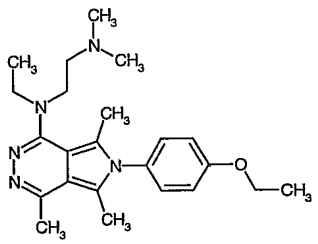
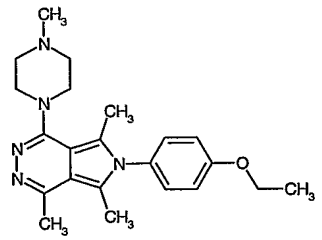
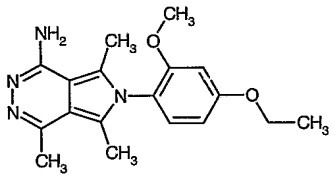
Example 343	N-(3-chloro-4-morpholin-4-ylphenyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		493
Example 344	6-(4-ethoxyphenyl)-1-[4-(4-fluorophenyl)piperazin-1-yl]-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		461
Example 345	1-(3,5-dimethylpiperidin-1-yl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		394
Example 346	6-(4-ethoxyphenyl)-N-(4-methoxybenzyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		418

Example 347	6-(4-ethoxyphenyl)-1-[4-(2-methoxyphenyl)piperazin-1-yl]-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		473
Example 348	N'-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-N,N-diethylpropane-1,3-diamine		411
Example 349	6-(4-ethoxyphenyl)-1-[4-(2-fluorophenyl)piperazin-1-yl]-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		461
Example 350	N-benzyl-6-(4-ethoxyphenyl)-N,4,5,7-tetramethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		402

Example 351	1-{4-[2-(4-chlorophenyl)ethyl]piperidin-1-yl}-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		504
Example 352	N~4~-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-N~1~,N~1~-diethylpentane-1,4-diamine		439
Example 353	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-[4-(trifluoromethyl)benzyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		455
Example 354	1-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-4-[3-(trifluoromethyl)phenyl]piperidin-4-ol		526

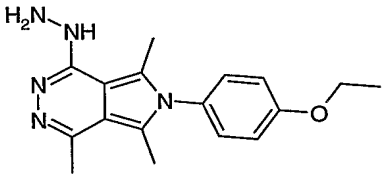
Example 355	N-[3,5-bis(trifluoromethyl)benzyl]-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		523
Example 356	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-[2-(1-methylpyrrolidin-2-yl)ethyl]-6H-pyrrolo[3,4-d]pyridazin-1-amine		409
Example 357	6-(4-ethoxyphenyl)-1,5,7-trimethyl-4-morpholin-4-yl-6H-pyrrolo[3,4-d]pyridazine		367
Example 358	6-(4-ethoxyphenyl)-1-[4-(2-furoyl)piperazin-1-yl]-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		461
Example 359	4-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]piperazine-1-carbaldehyde		394

Example 360	6-(4-ethoxyphenyl)-1,5,7-trimethyl-4-(4-methylpiperazin-1-yl)-6H-pyrrolo[3,4-d]pyridazine		381
Example 361	1-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine		396
Example 362	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-(pyridin-2-ylmethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		388
Example 363	6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-(2-pyrrolidin-1-ylethyl)-6H-pyrrolo[3,4-d]pyridazin-1-amine		395
Example 364	1-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-N,N-diethylpiperidine-3-carboxamide		465

Example 365	N-[6-(4-ethoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]-N-ethyl-N',N'-dimethylethane-1,2-diamine		397
Example 366	6-(4-ethoxyphenyl)-1,5,7-trimethyl-4-(4-methylpiperazin-1-yl)-6H-pyrrolo[3,4-d]pyridazine		381
Example 367	6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-amine		327

EXAMPLE 368

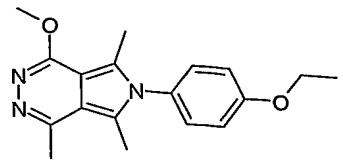
6-(4-ethoxyphenyl)-1-hydrazino-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazine



Utilizing the general procedure outlined in **EXAMPLE 85**, 1-chloro-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine and hydrazine (0.10mL, 0.32mmol) reacted to give 6-(4-ethoxyphenyl)-1-hydrazino-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.03-7.11 (m, 4H), 4.12 (q, 2H), 2.43 (s, 3H), 2.36 (s, 3H), 2.28 (s, 3H), 1.69 (s, 2H), 1.50 (t, 3H); MS (ESI) 312 $(M+H)^+$.

EXAMPLE 369

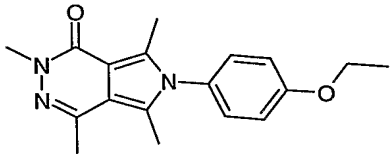
6-(4-ethoxyphenyl)-1-methoxy-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



A solution of 1-chloro-6-(4-ethoxyphenyl)-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine (**EXAMPLE 85**) (100mg, 0.32mmol) and MeOH (5mL) was treated with a solution of NaOMe (freshly prepared from MeOH (5mL) and sodium metal (22mg, 0.96mmol)). The resulting mixture was placed in a resealable reaction vessel and heated at 100°C for 12h. The reaction was allowed to cool to rt, and poured into ice water (100mL) to give 6-(4-ethoxyphenyl)-1-methoxy-4,5,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.11-7.25 (m, 4H), 4.16 (q, 2H), 2.71 (s, 3H), 2.40 (s, 3H), 2.38 (s, 3H), 1.43-1.46 (t, 3H); MS (ESI) 312 $(M+H)^+$.

EXAMPLE 370

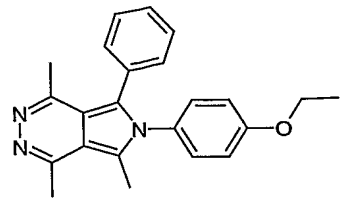
6-(4-ethoxyphenyl)-2,4,5,7-tetramethyl-2,6-dihydro-1*H*-pyrrolo[3,4-*d*]pyridazin-1-one



A solution of ethyl-4-acetyl-1-(4-ethoxyphenyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (prepared as in **EXAMPLE 85**) (70mg, 0.20mmol) and MeOH (5mL) in a resealable reaction vessel was mixed with methylhydrazine (0.032 mL, 0.60 mmol) and AcOH (~3 drops). The vessel was sealed and heated at 70°C for 12h. The resulting slurry was allowed to cool to rt and poured into ice water (50mL). The resulting white solid was filtered and dried under vacuum for 8h to give 6-(4-ethoxyphenyl)-2,4,5,7-tetramethyl-2,6-dihydro-1*H*-pyrrolo[3,4-*d*]pyridazin-1-one: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.00-7.26 (m, 4H), 4.10 (q, 2H), 3.71 (s, 3H), 2.49 (s, 3H), 2.45 (s, 3H), 2.30 (s, 3H), 1.48 (t, 3H); MS (ESI) 312 $(M+H)^+$.

EXAMPLE 371

6-(4-ethoxyphenyl)-5-phenyl-1,4,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine



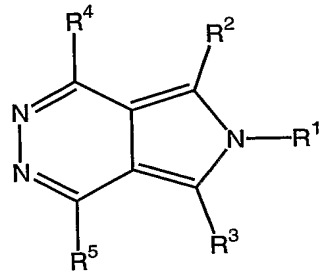
To a solution of 1-phenyl-1,4-pentanedione (1.06g, 6.0mmol) and toluene (50mL) was added *p*-phenetidine (0.78mL, 6.0mmol) and 5 drops of glacial acetic acid. The mixture was heated at reflux overnight. After cooling to rt, the mixture was concentrated *in vacuo* and purified by flash chromatography on silica gel (15–25% EtOAc/hexanes) to give 1-(*p*-ethoxyphenyl)-5-methyl-2-phenyl-pyrrole as a yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.17 – 7.13 (m, 2H), 7.10 – 7.05 (m, 5H), 6.89 – 6.84 (m, 2H), 6.35 (d, 1H), 6.08 (d, 1H), 4.04 (q, 2H), 2.13 (s, 3H), 1.44 (t, 3H); MS (ESI) 278 $(M + H)^+$.

Acetyl chloride (0.36mL, 5.0mmol) and $SnCl_4$ (5.0mL of a 1.0M solution in CH_2Cl_2, 5.0mmol) were added dropwise to a stirring solution of 1-(*p*-ethoxyphenyl)-5-methyl-2-phenyl-pyrrole (554mg, 2.0mmol) and toluene (10mL) at 0°C. The mixture was warmed to rt and then heated at 50°C overnight. Following cooling to rt, the mixture was diluted with 1N NaOH (50mL), extracted with EtOAc (100mL), the organic layer washed with brine, dried ($MgSO_4$), filtered, concentrated *in vacuo*, and purified by flash chromatography on silica gel (0–30% EtOAc/hexanes). The resulting diacetylpyrrole was dissolved in EtOH (10mL) and hydrazine (0.5mL) and the mixture was heated at 50°C for 2h. The mixture was cooled to rt and poured into ice water (50mL). The resulting solid was filtered to give 6-(4-ethoxyphenyl)-5-phenyl-1,4,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.26 – 7.23 (m, 3H), 7.16 – 7.13 (m, 2H), 7.00 – 6.97 (m, 2H), 6.84 – 6.81 (m, 2H), 3.99 (q, 2H), 2.87 (s, 3H), 2.53 (s, 3H), 2.27 (s, 3H), 1.40 (t, 3H); MS $(M + H)^+$ 358.58.

Other variations or modifications, which will be obvious to those skilled in the art, are within the scope and teachings of this invention. This invention is not to be limited except as set forth in the following claims.

WHAT IS CLAIMED IS:

1. A method of binding the $\alpha 2\delta$ subunit of voltage gated calcium channels comprising a step of administering an effective amount of a compound represented by Formula (I):



(I)

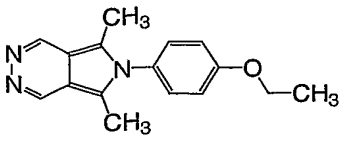
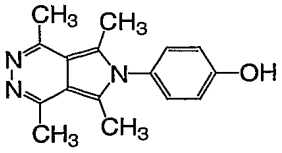
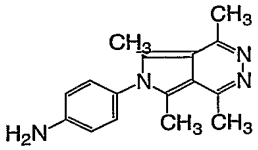
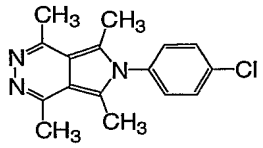
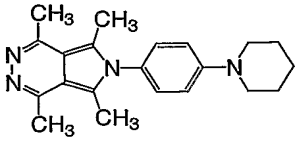
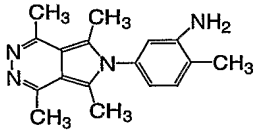
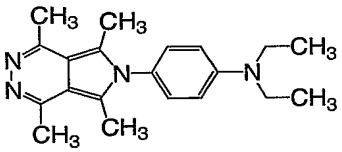
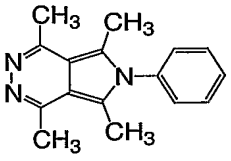
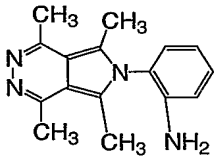
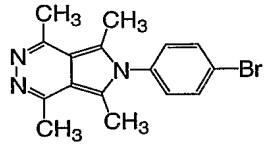
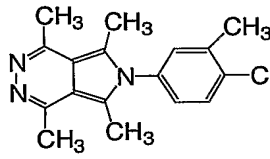
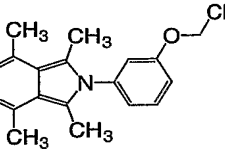
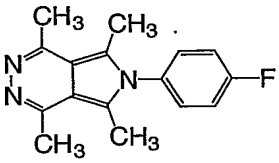
or a pharmaceutically acceptable salt thereof, wherein

R^1 is $-C_{0-6}$alkyl–aryl, $-C_{0-6}$alkyl–heteroaryl, $-C_{0-6}$alkyl–C_{3-6}cycloalkyl, or $-C_{0-6}$alkyl–heteroC_{3-7}cycloalkyl, optionally substituted with 1-6 independent halogen, –CN, NO_2, -C_{1-6}alkyl, $-C_{0-6}$alkyl–C_{3-6}cycloalkyl, $-C_{0-6}$alkyl–heteroC_{3-7}cycloalkyl, $-OR^6$, $-NR^6R^7$, $-C(=NR^6)NR^7R^8$, $-N(-NR^{88}R^6)NR^7R^8$, $-NR^6COR^7$, $-NR^6CO_2R^7$, $-NR^6SO_2R^{88}$, $-NR^6CONR^7R^8$, $-SR^{88}$, $-SOR^{88}$, $-SO_2R^{88}$, $-SO_2NR^6R^7$, $-COR^6$, $-CO_2R^6$, $-CONR^6R^7$, $-C(=NR^6)R^7$, or $-C(=NOR^6)R^7$ substituents;

R^2, R^4, R^3, and R^5 each independently is $-C_{0-6}$alkyl, $-C_{0-6}$alkyl–aryl, $-C_{0-6}$alkyl–heteroaryl, $-C_{0-6}$alkyl–C_{3-6}cycloalkyl, or $-C_{0-6}$alkyl–heteroC_{3-7}cycloalkyl, optionally substituted with 1-6 independent halogen, –CN, NO_2, -C_{1-6}alkyl, $-OR^6$, $-NR^6R^7$, $-C(=NR^6)NR^7R^8$, $-N(-NR^{88}R^6)NR^7R^8$, $-NR^6COR^7$, $-NR^6CO_2R^7$, $-NR^6SO_2R^{88}$, $-NR^6CONR^7R^8$, $-SR^{88}$, $-SOR^{88}$, $-SO_2R^{88}$, $-SO_2NR^6R^7$, $-COR^6$, $-CO_2R^6$, $-CONR^6R^7$, $-C(=NR^6)R^7$, or $-C(=NOR^6)R^7$ substituents; and

R^6, R^7, R^8, and R^{88} each independently is $-C_{0-6}$alkyl, $-C_{3-7}$cycloalkyl, heteroaryl, or aryl; optionally substituted with 1-5 independent halogen, –CN, $-C_{1-6}$alkyl, $-O(C_{0-6}$alkyl), $-O(C_{3-7}$cycloalkyl), -O(aryl), $-N(C_{0-6}$alkyl)(C_{0-6}alkyl), $-N(C_{0-6}$alkyl)(C_{3-7}cycloalkyl), or $-N(C_{0-6}$alkyl)(aryl) substituents; and

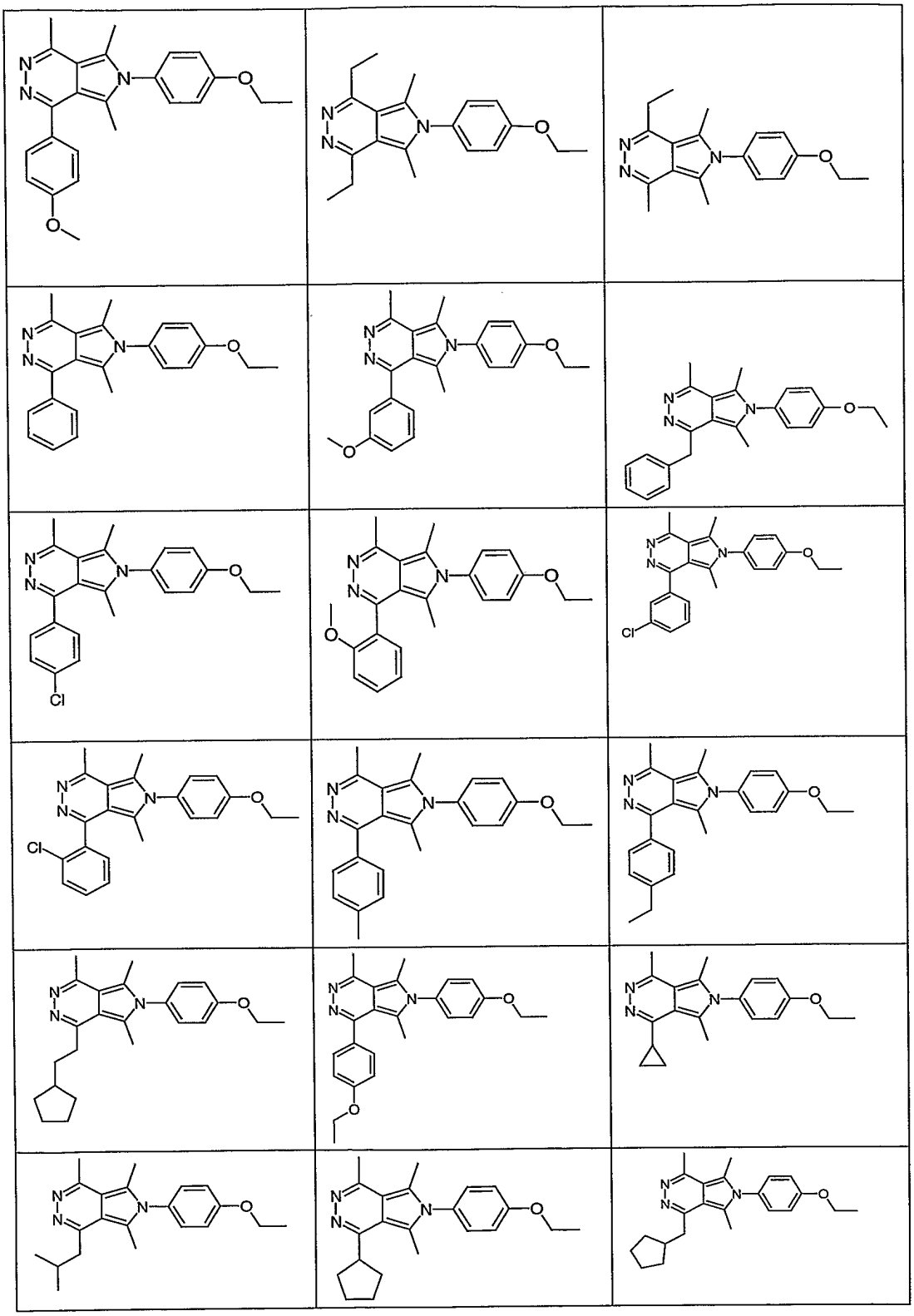
provided that the compound is not selected from the following table:

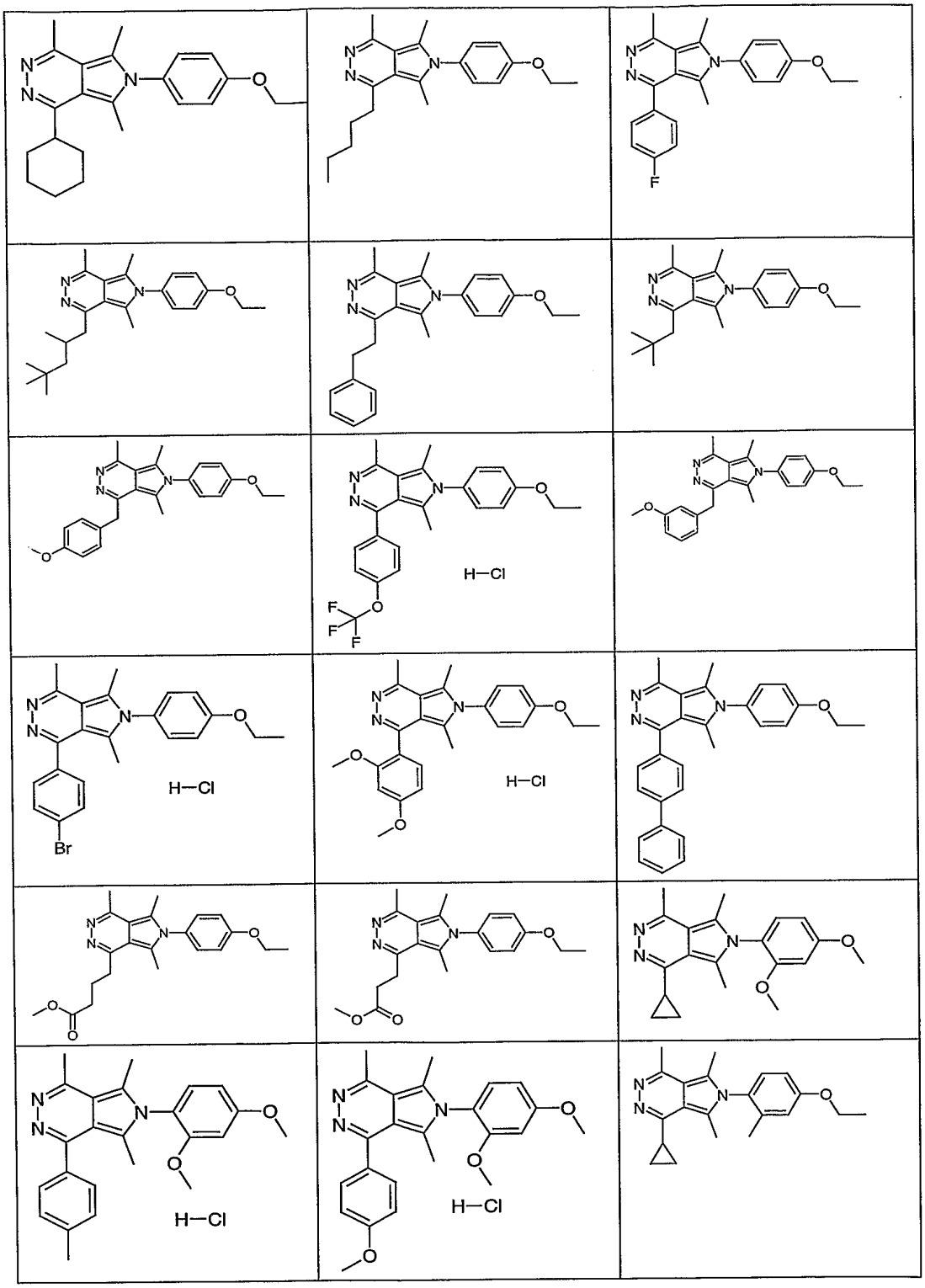
		
		
		
		
		

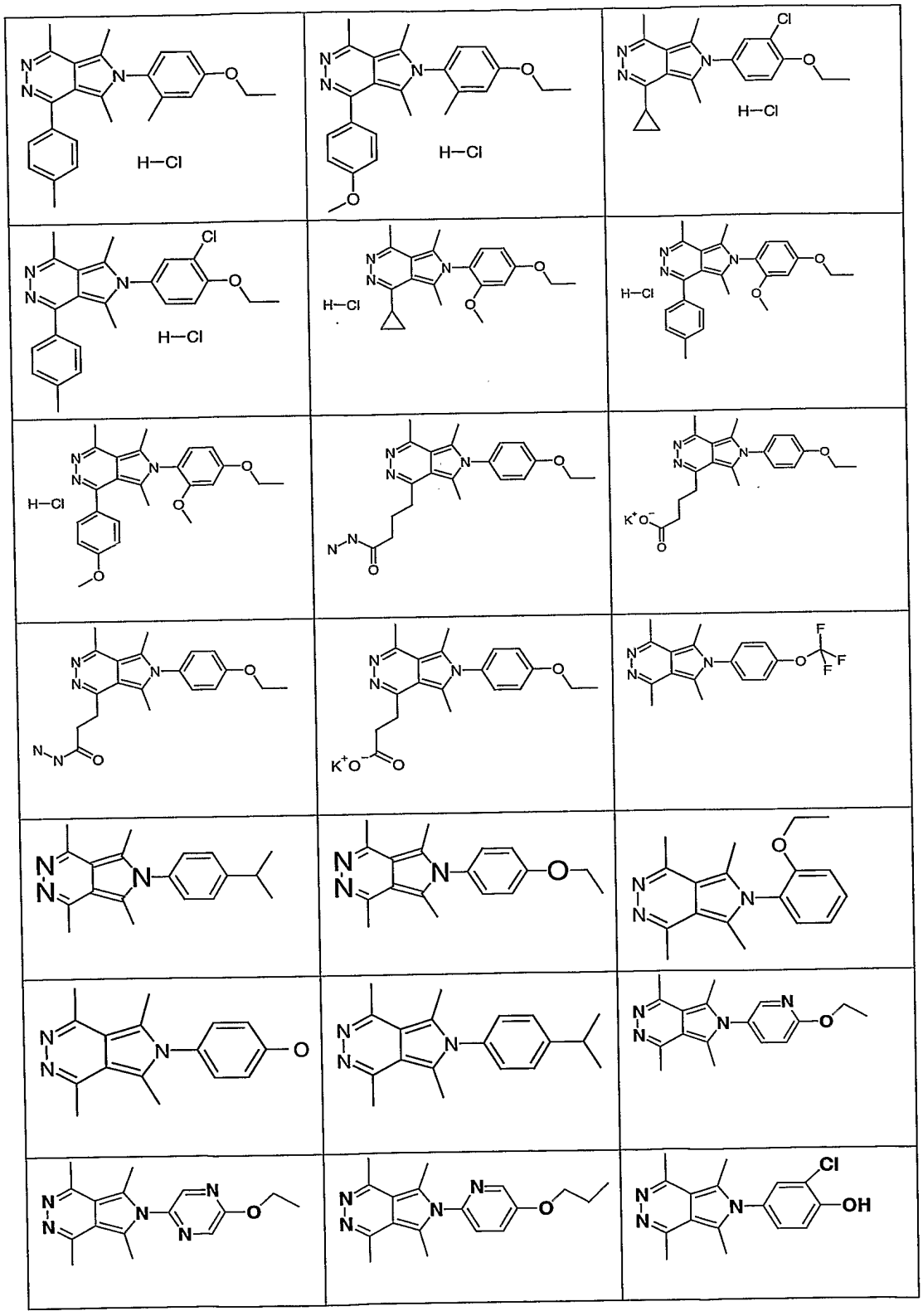
2. The method according to Claim 1, wherein R^1 is $-C_{0-6}$alkyl–aryl.

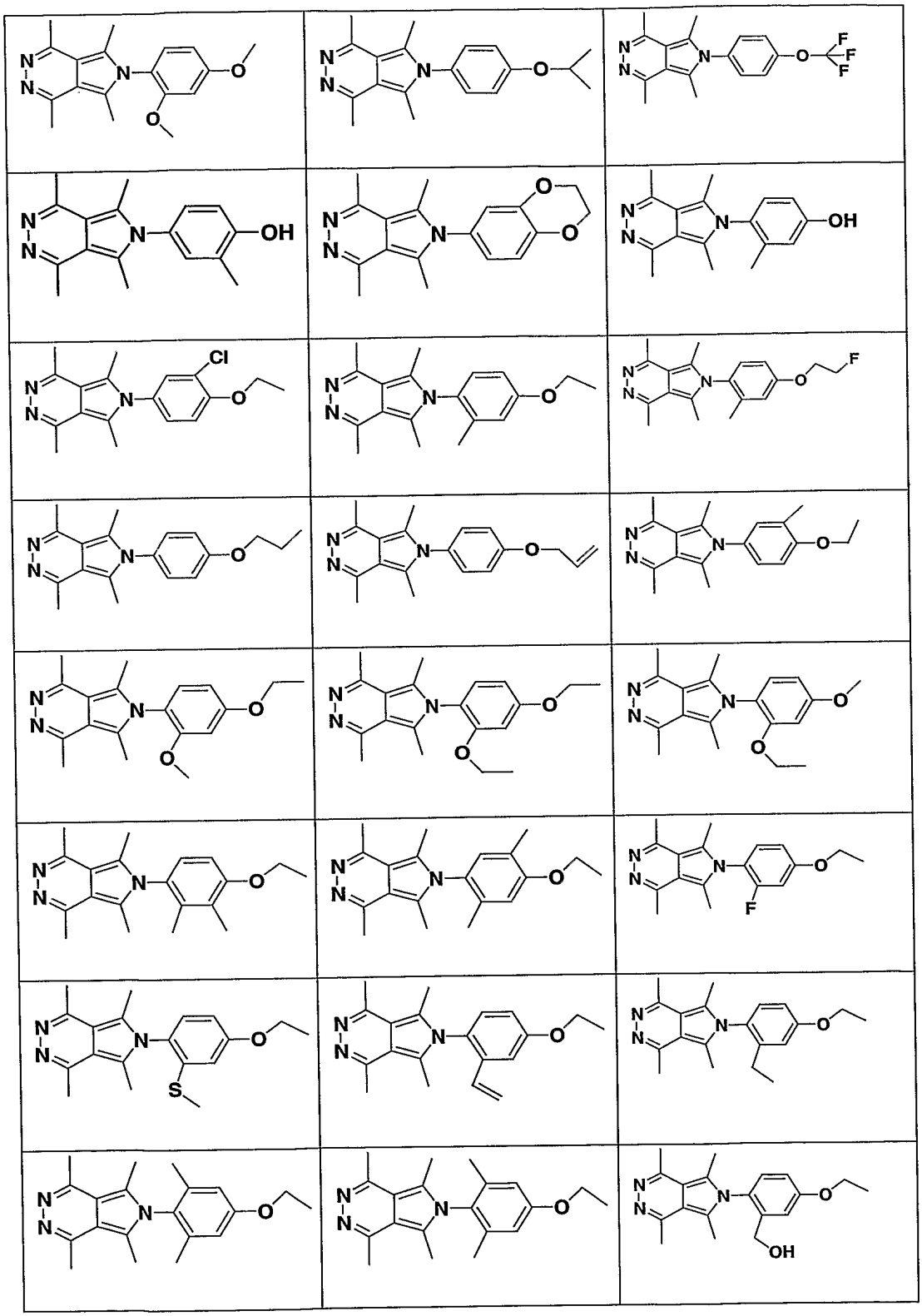
3. The method according to Claim 2, wherein R^1 is $-C_{0-6}$alkyl–phenyl.

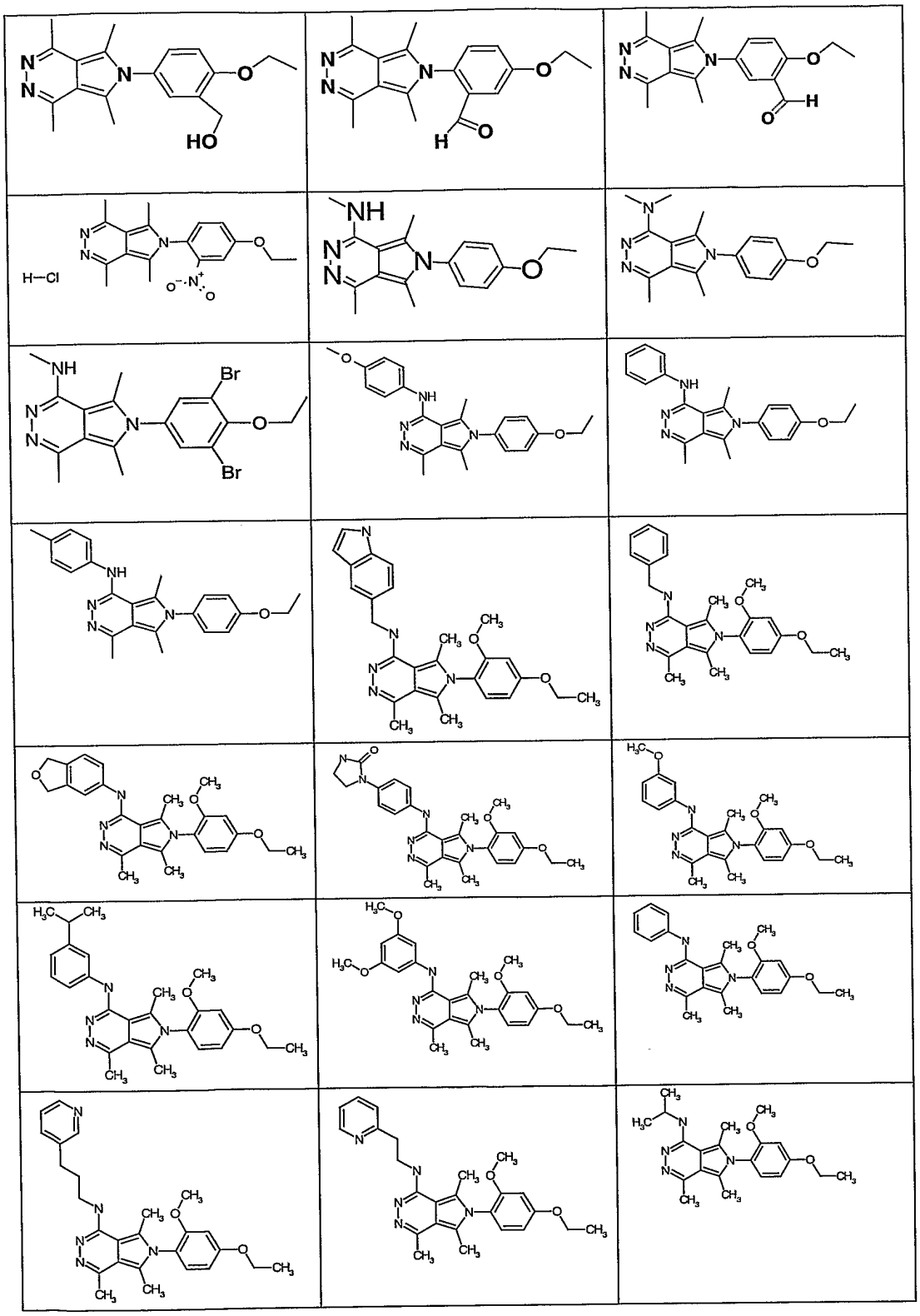
4. The method according to Claim 1, wherein the compound is selected from:

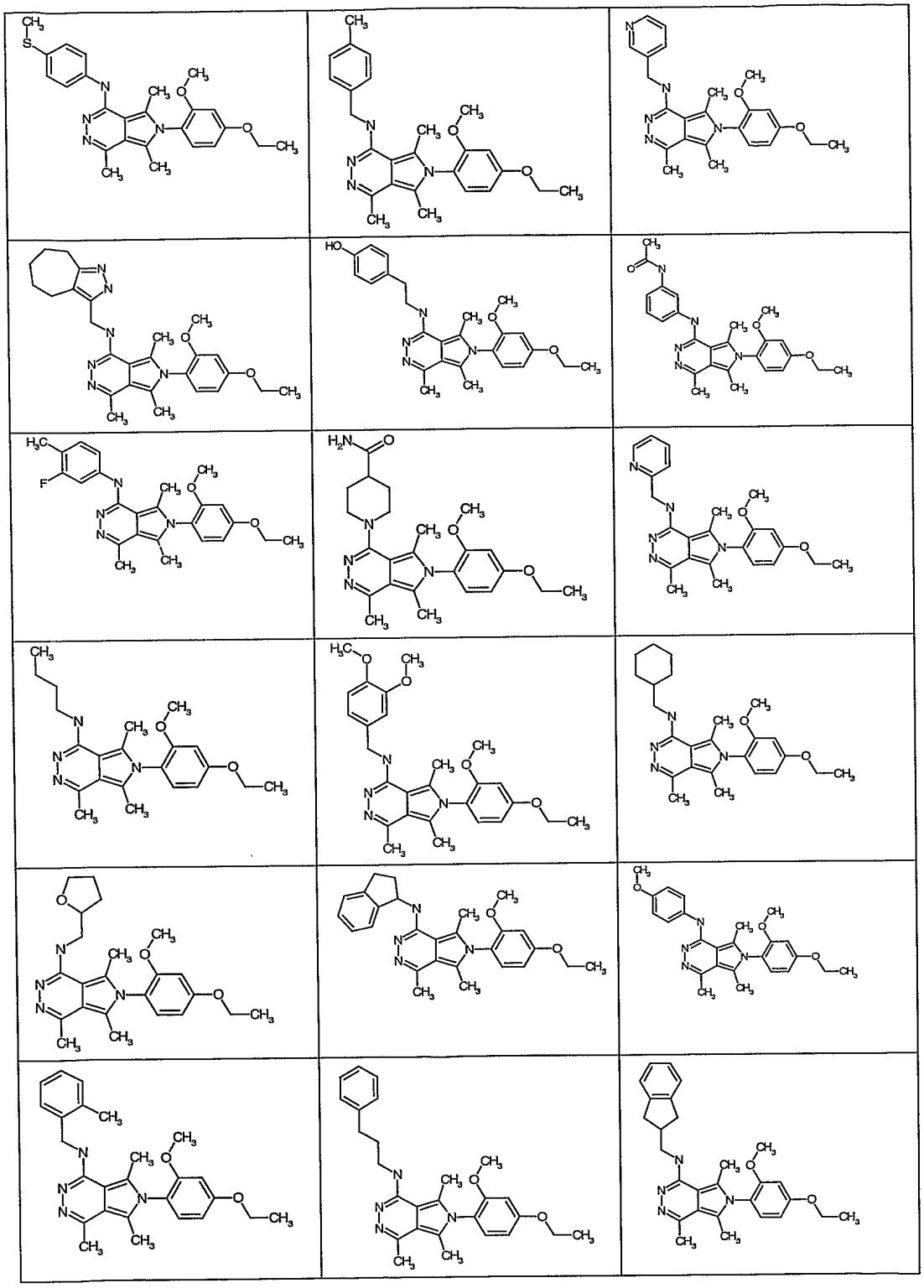


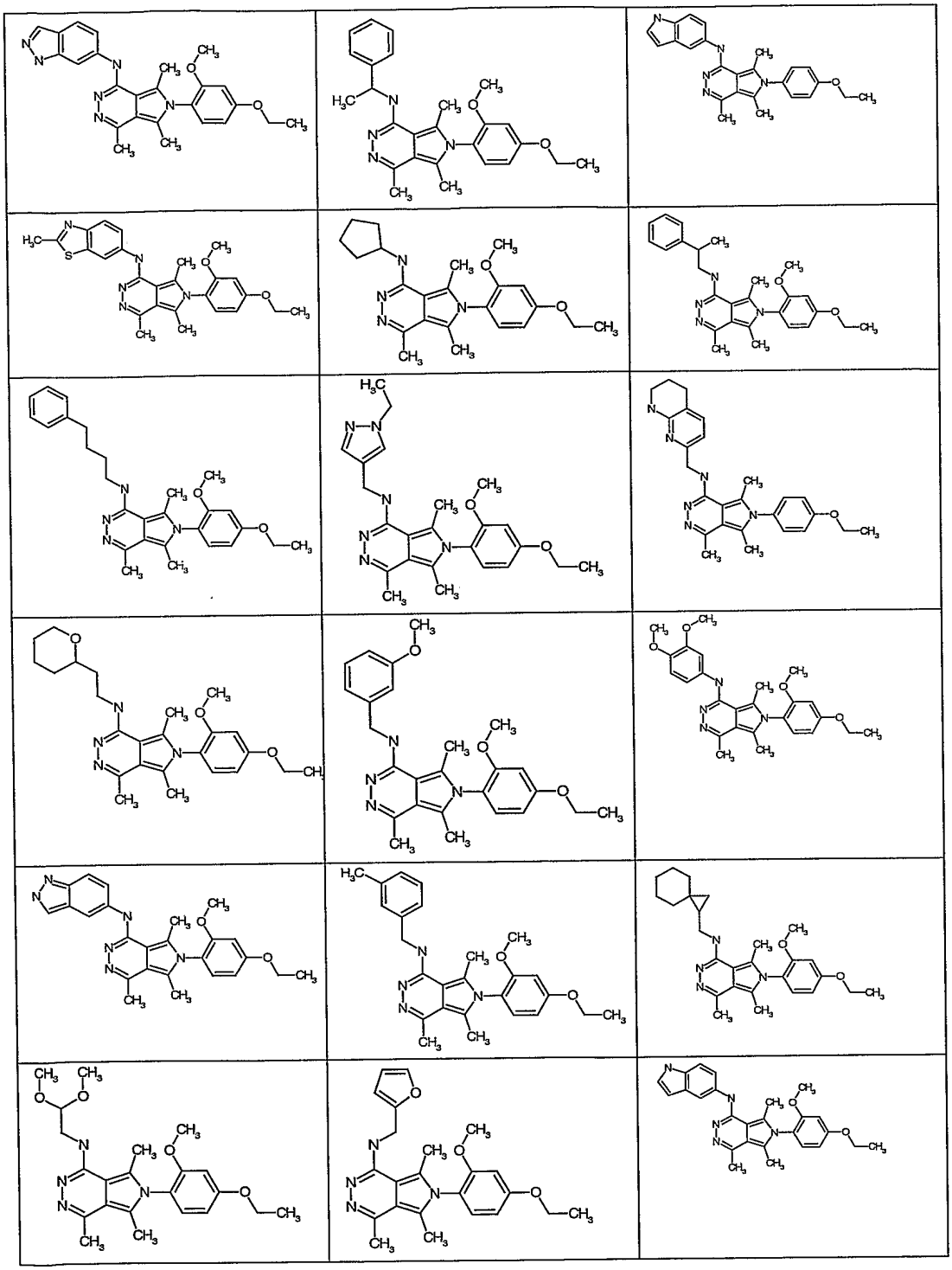

F
H—Cl
F
F
F
H—Cl
Br
H—Cl
H—Cl
H—Cl

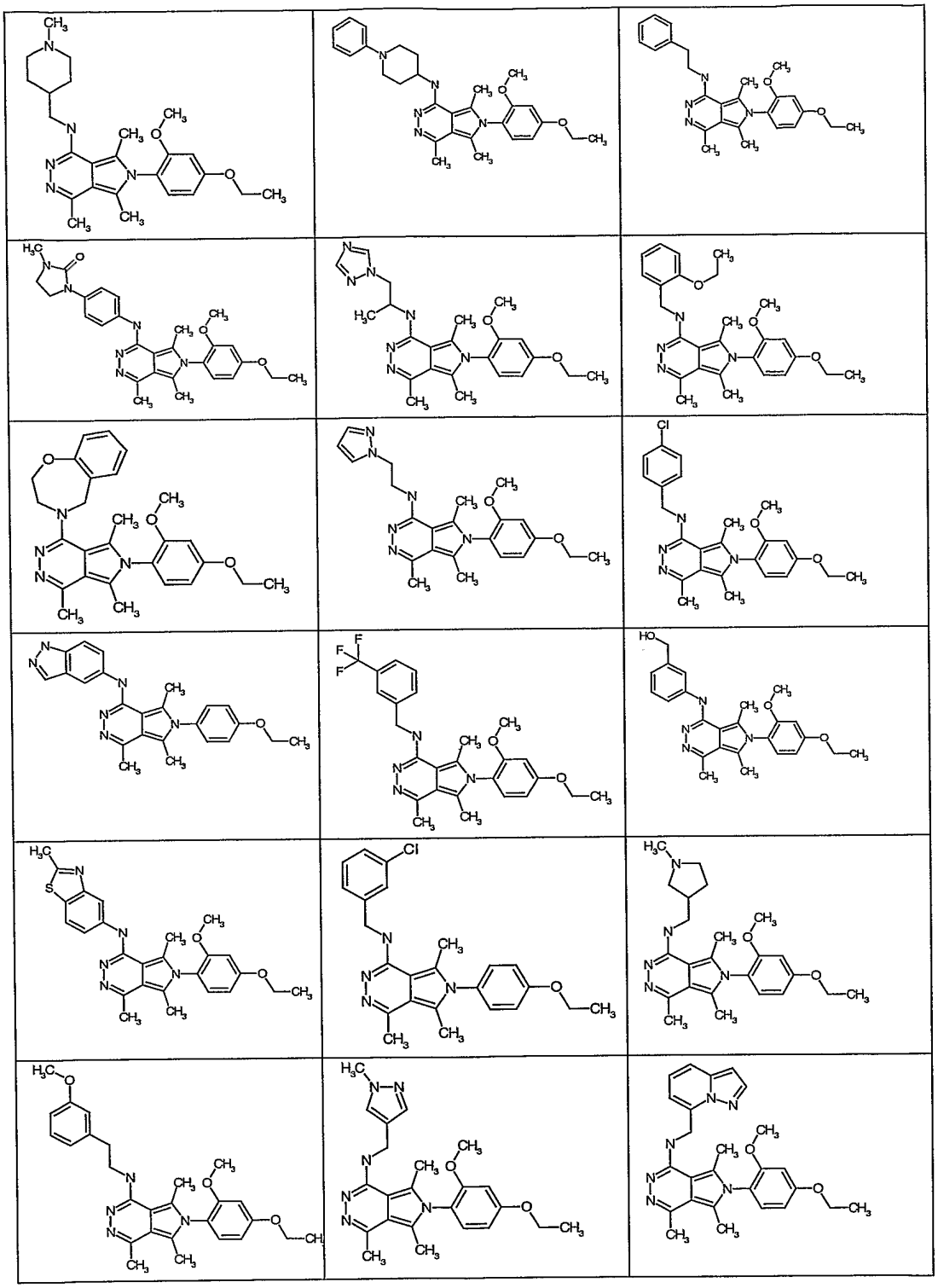


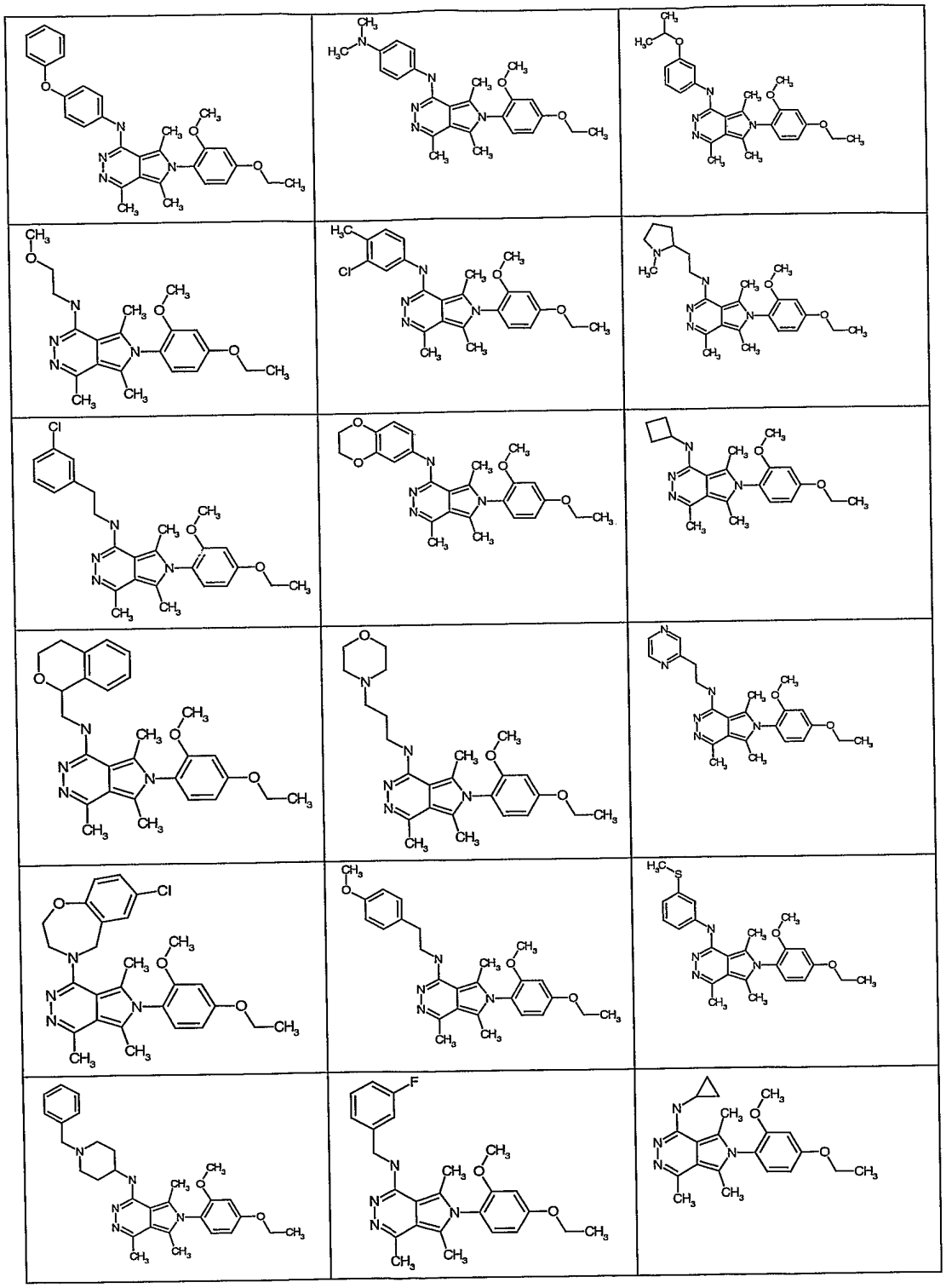


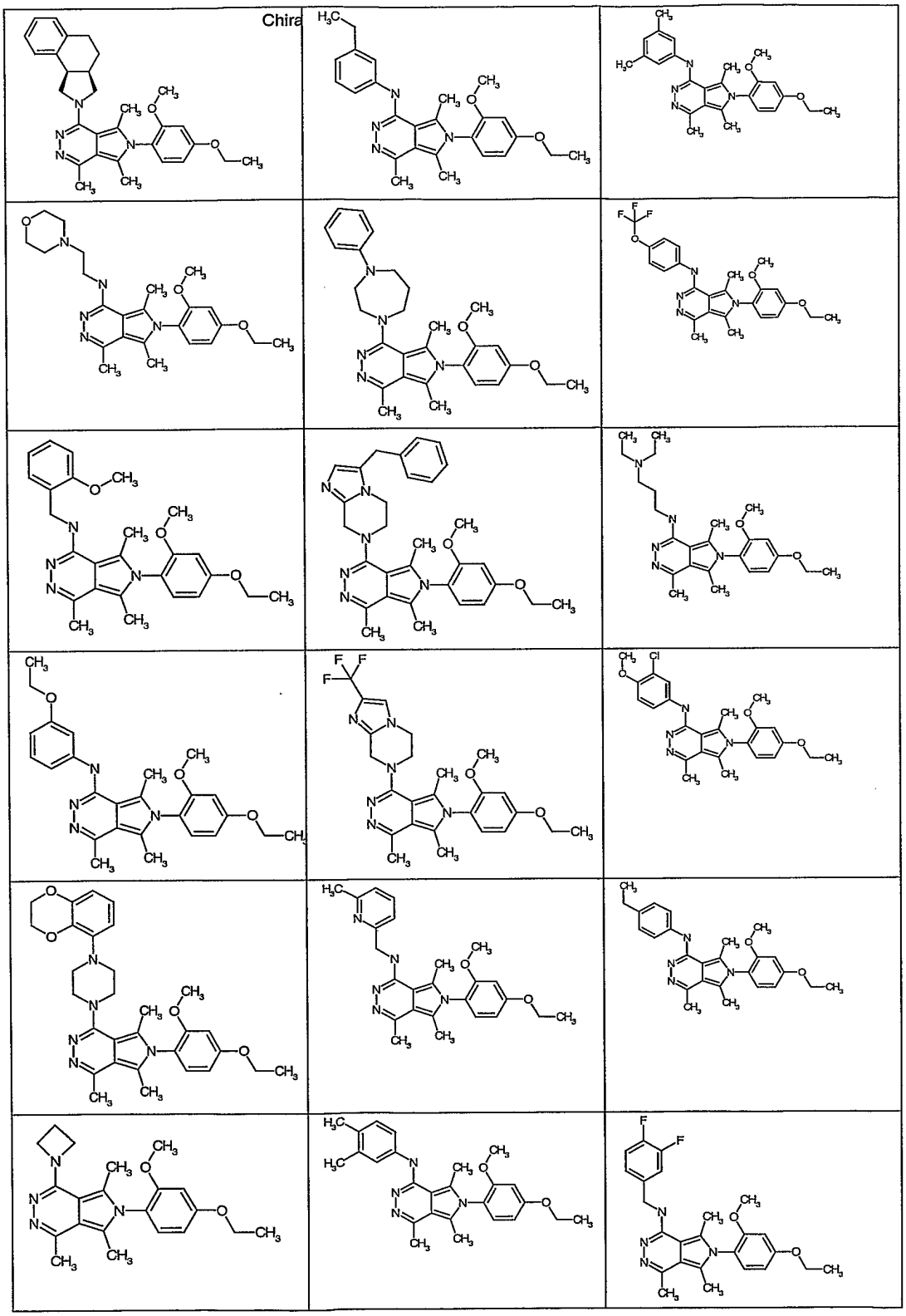


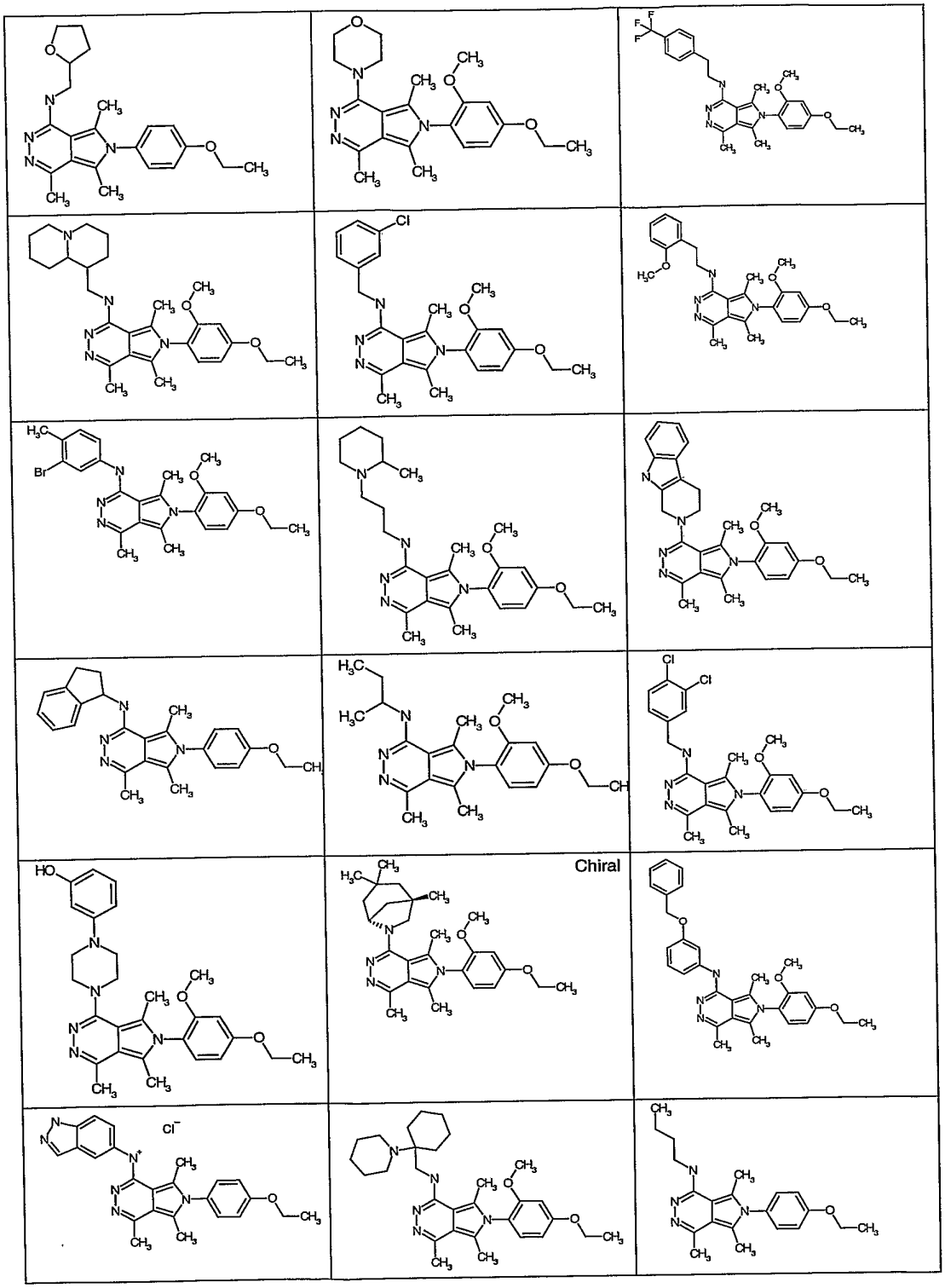









Chira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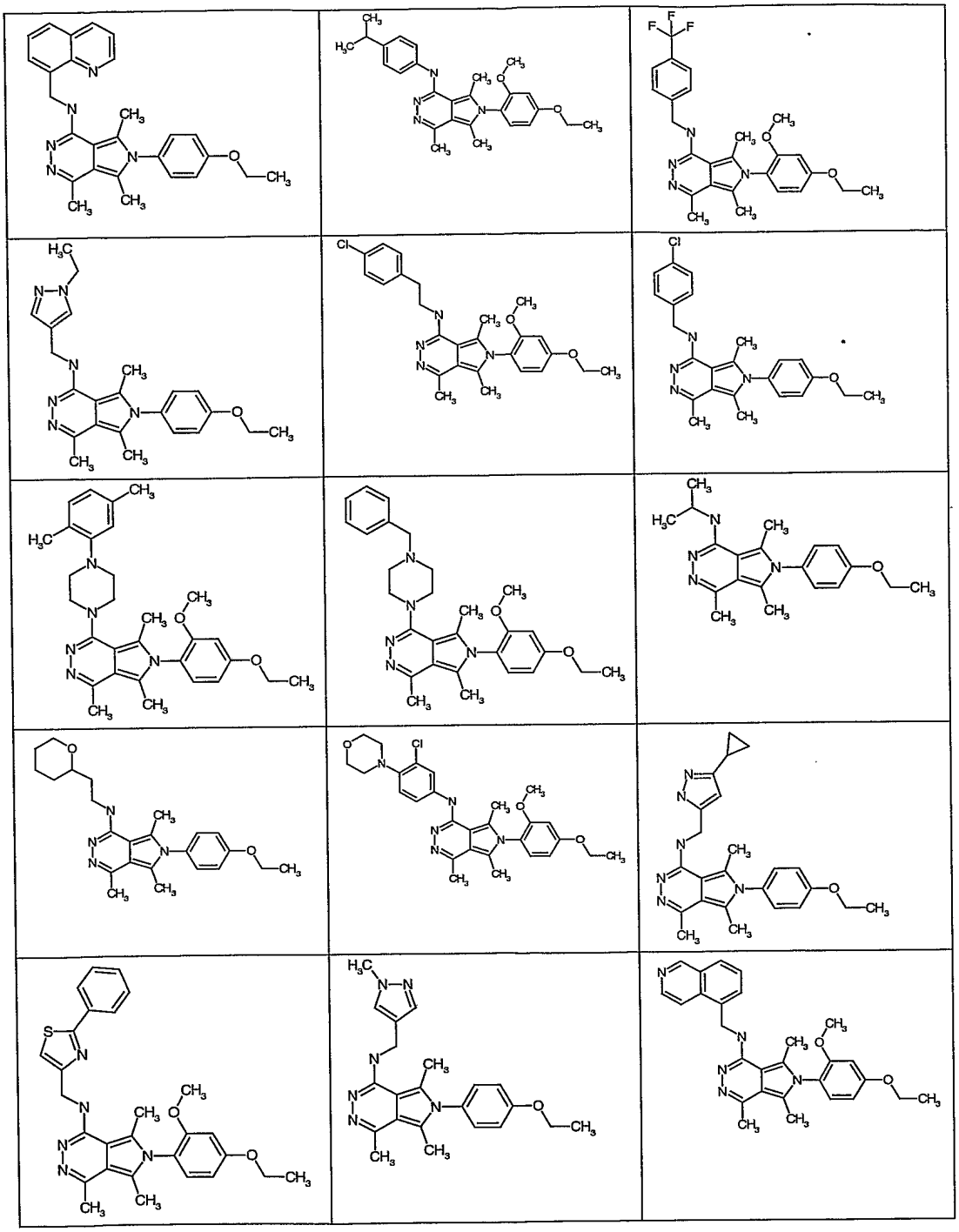
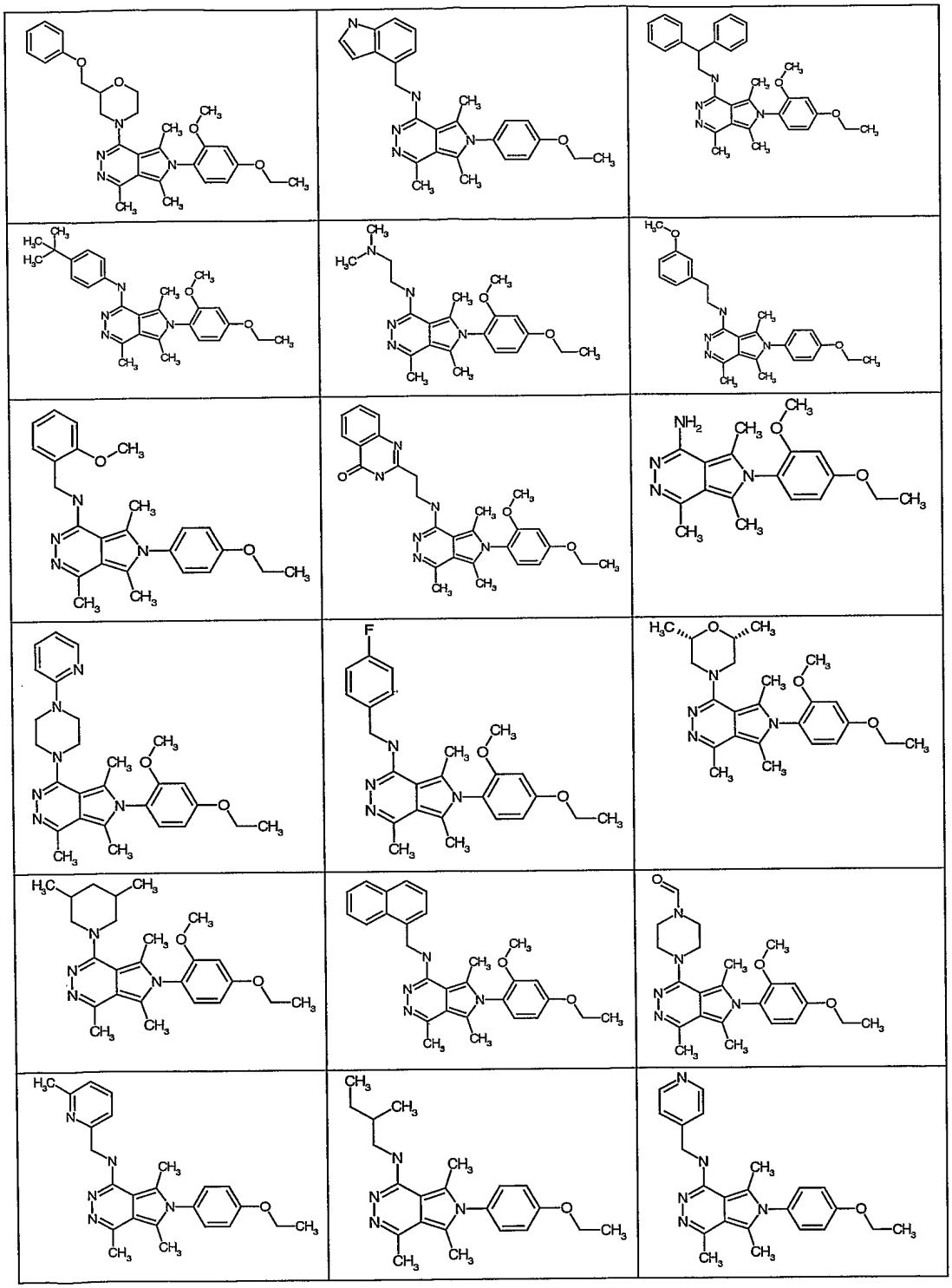
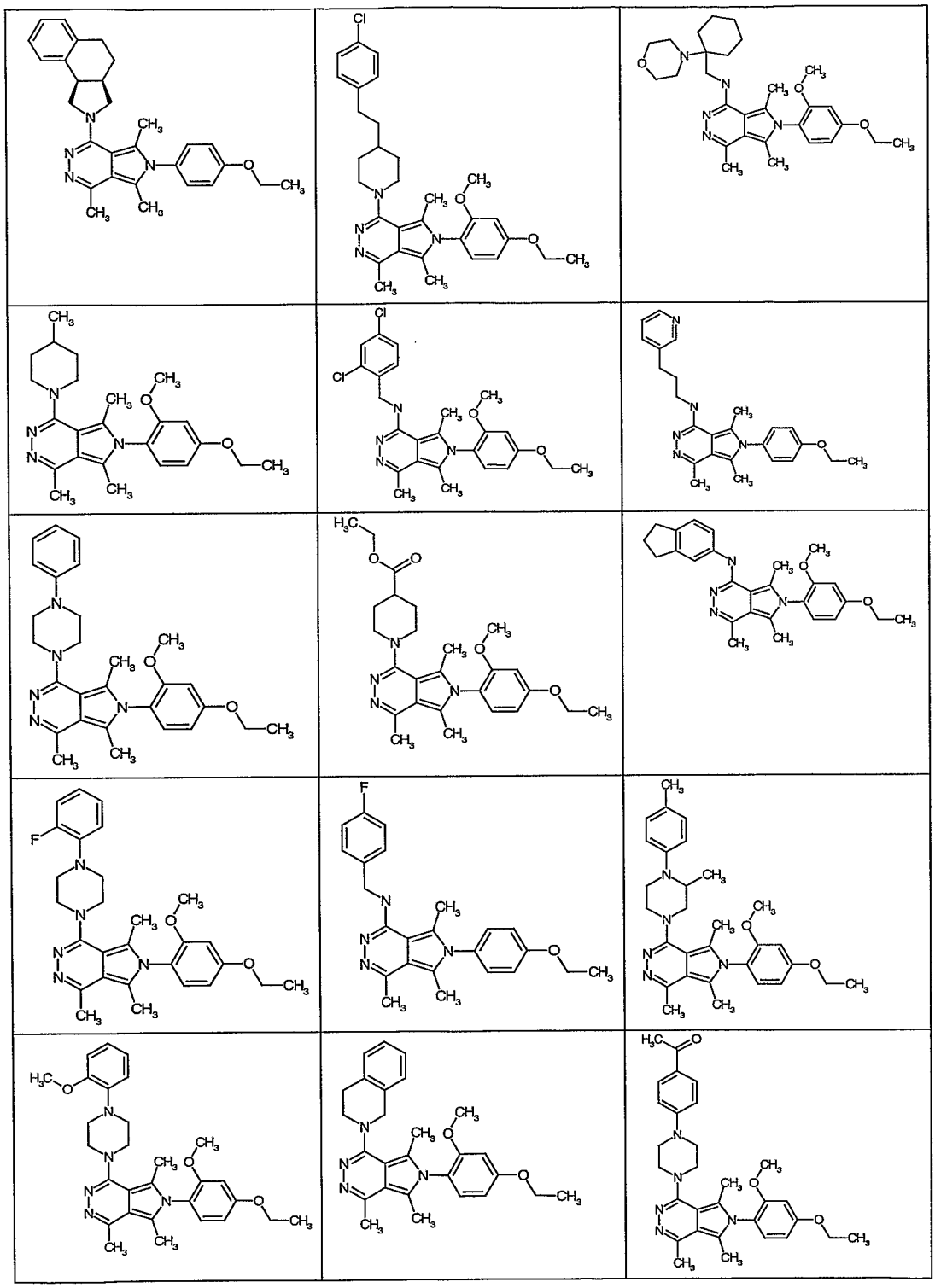
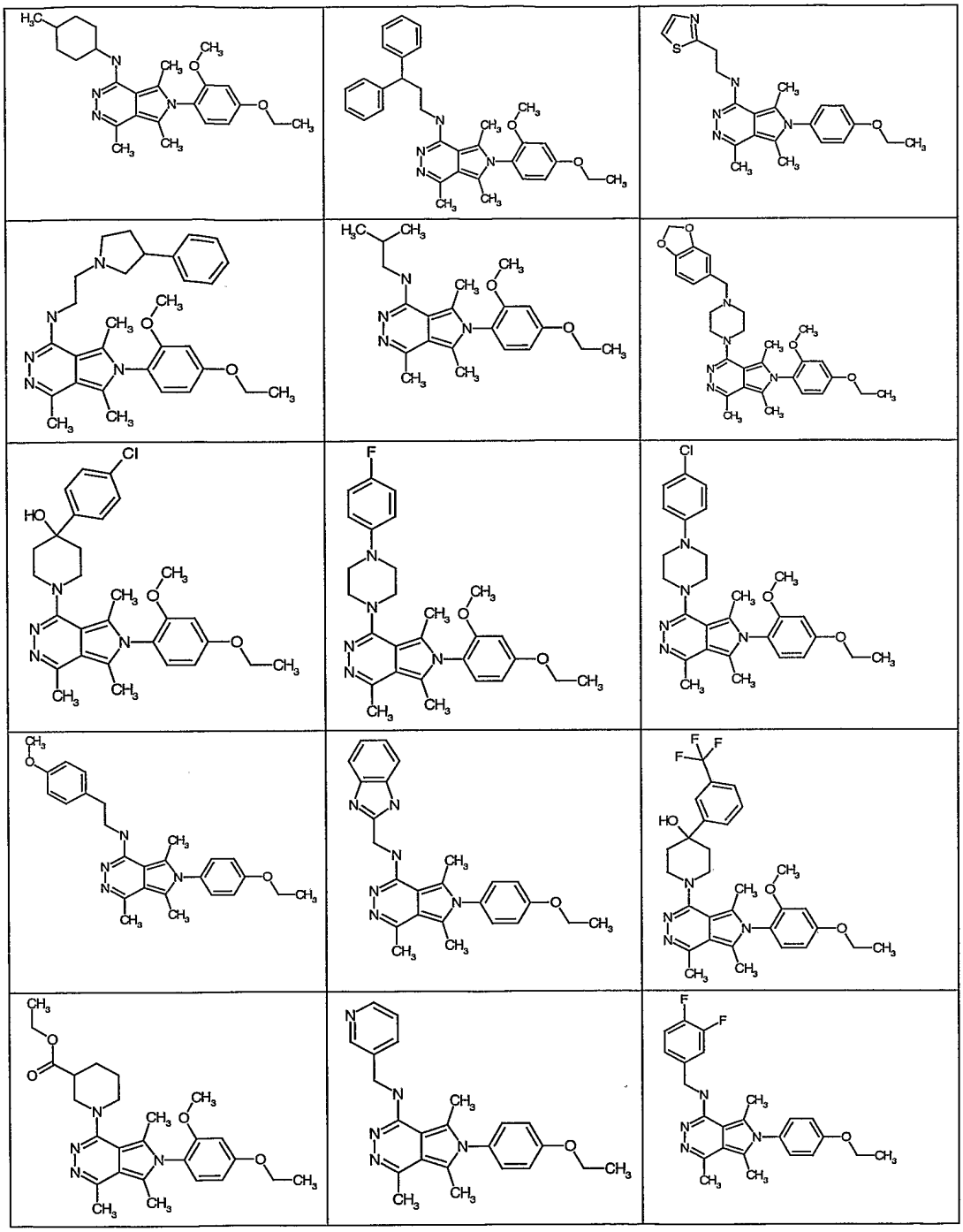
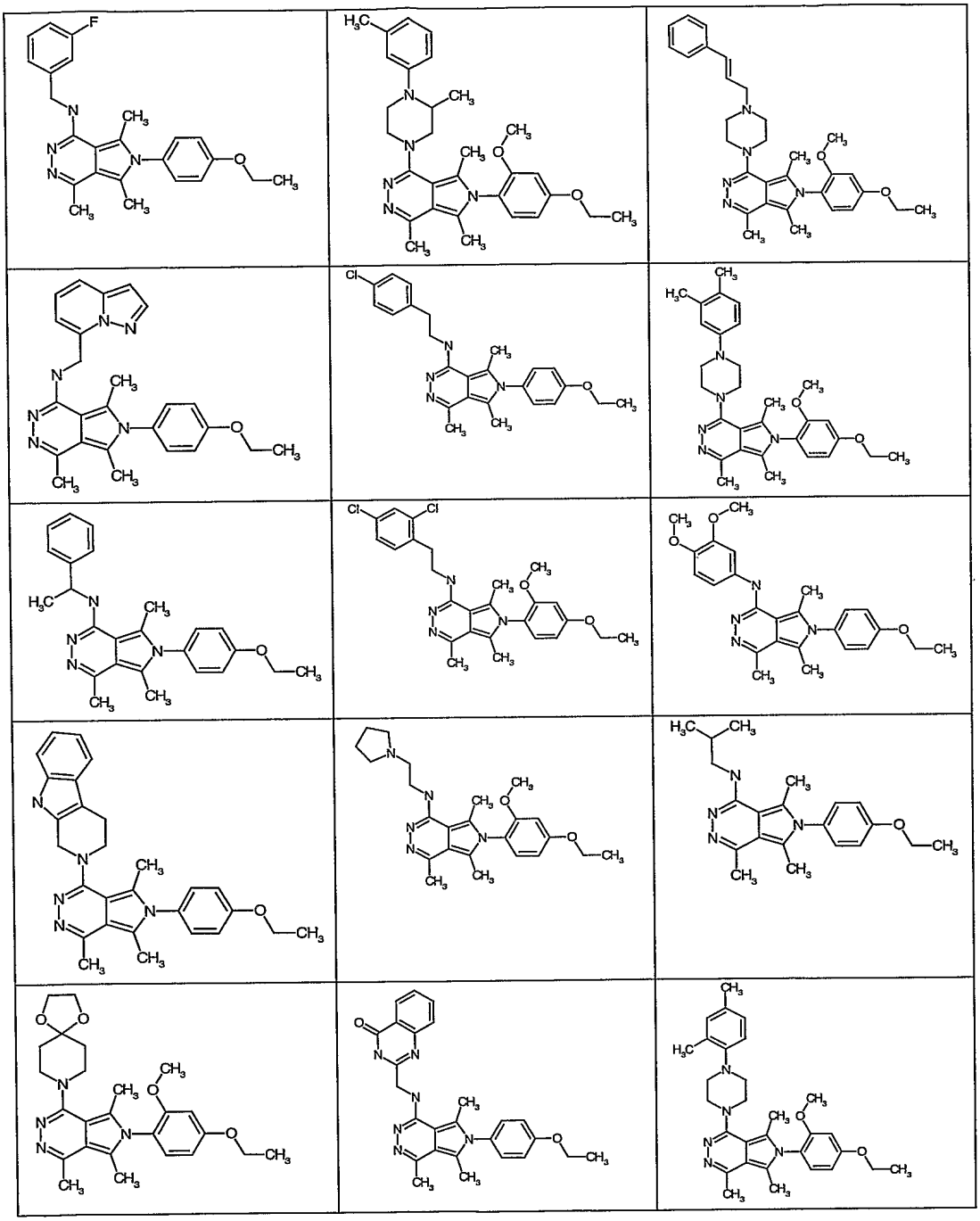
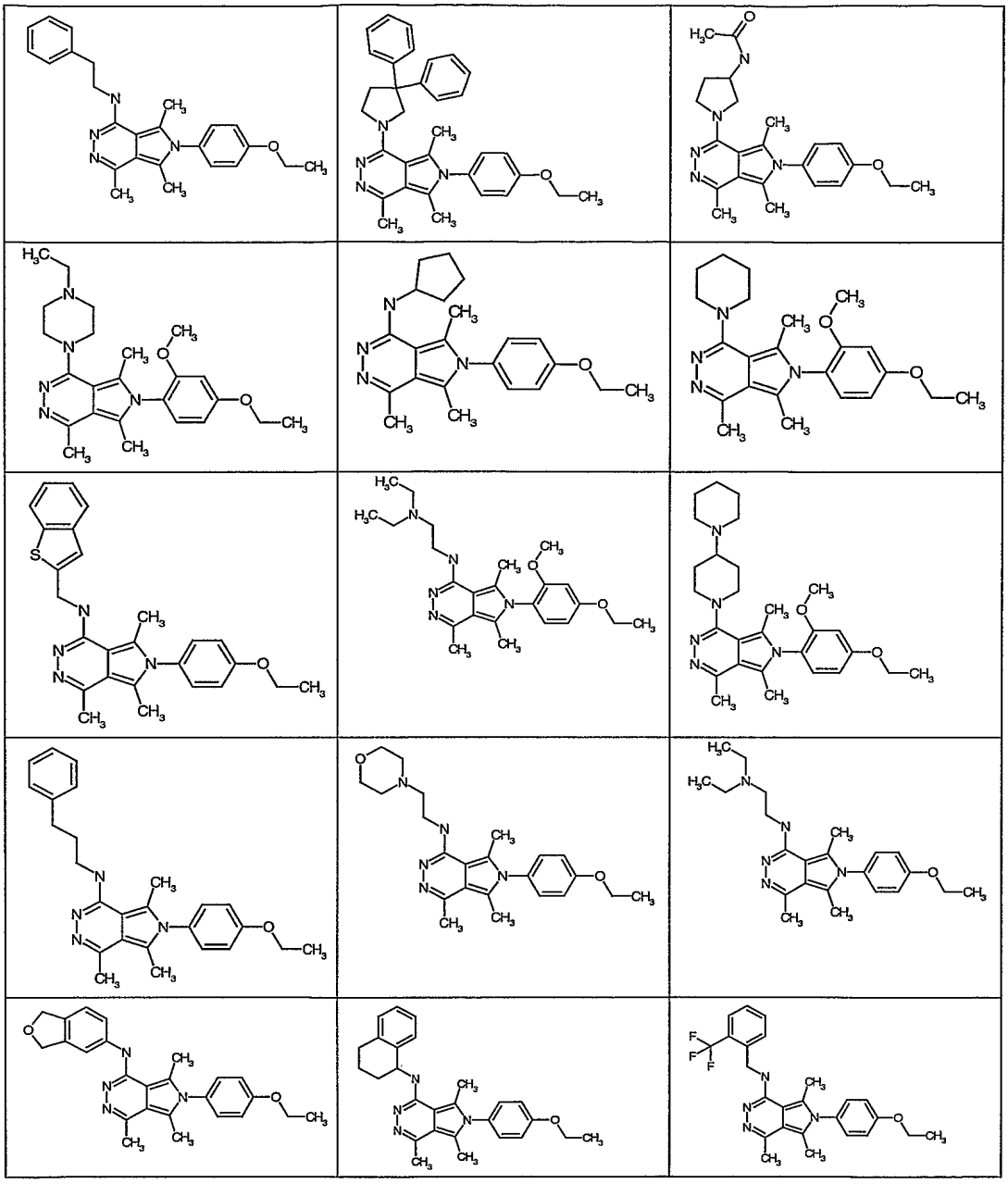


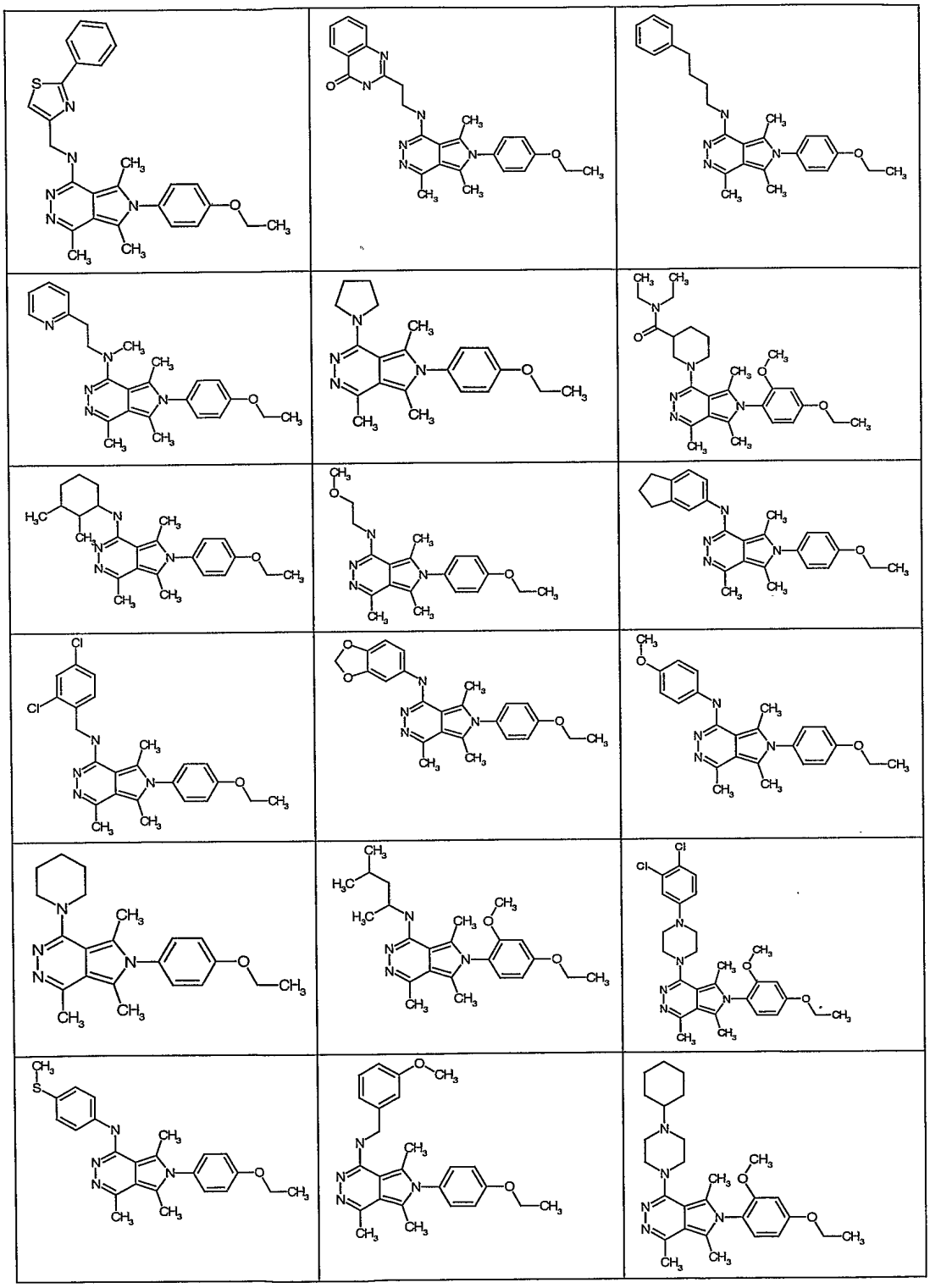


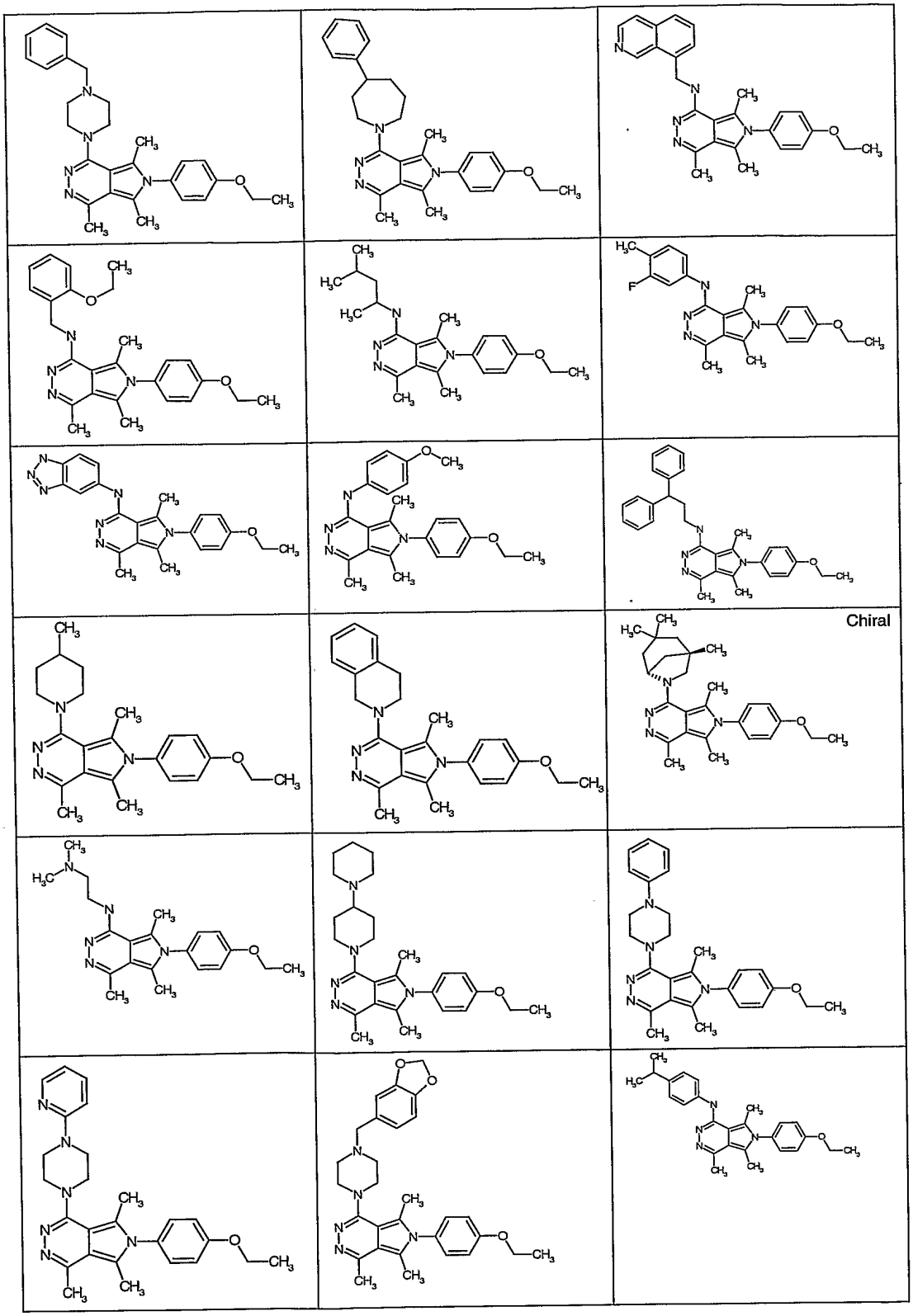


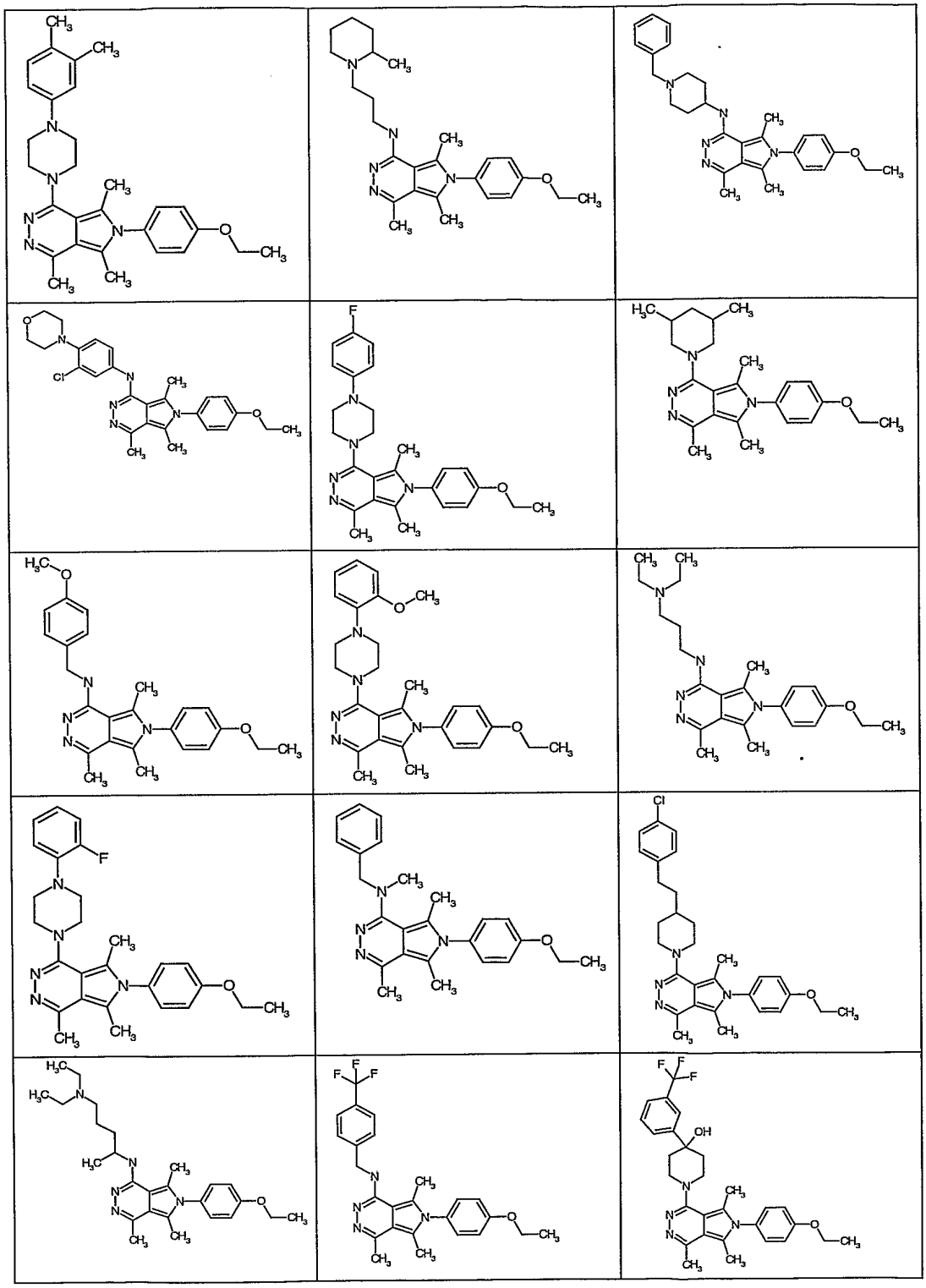


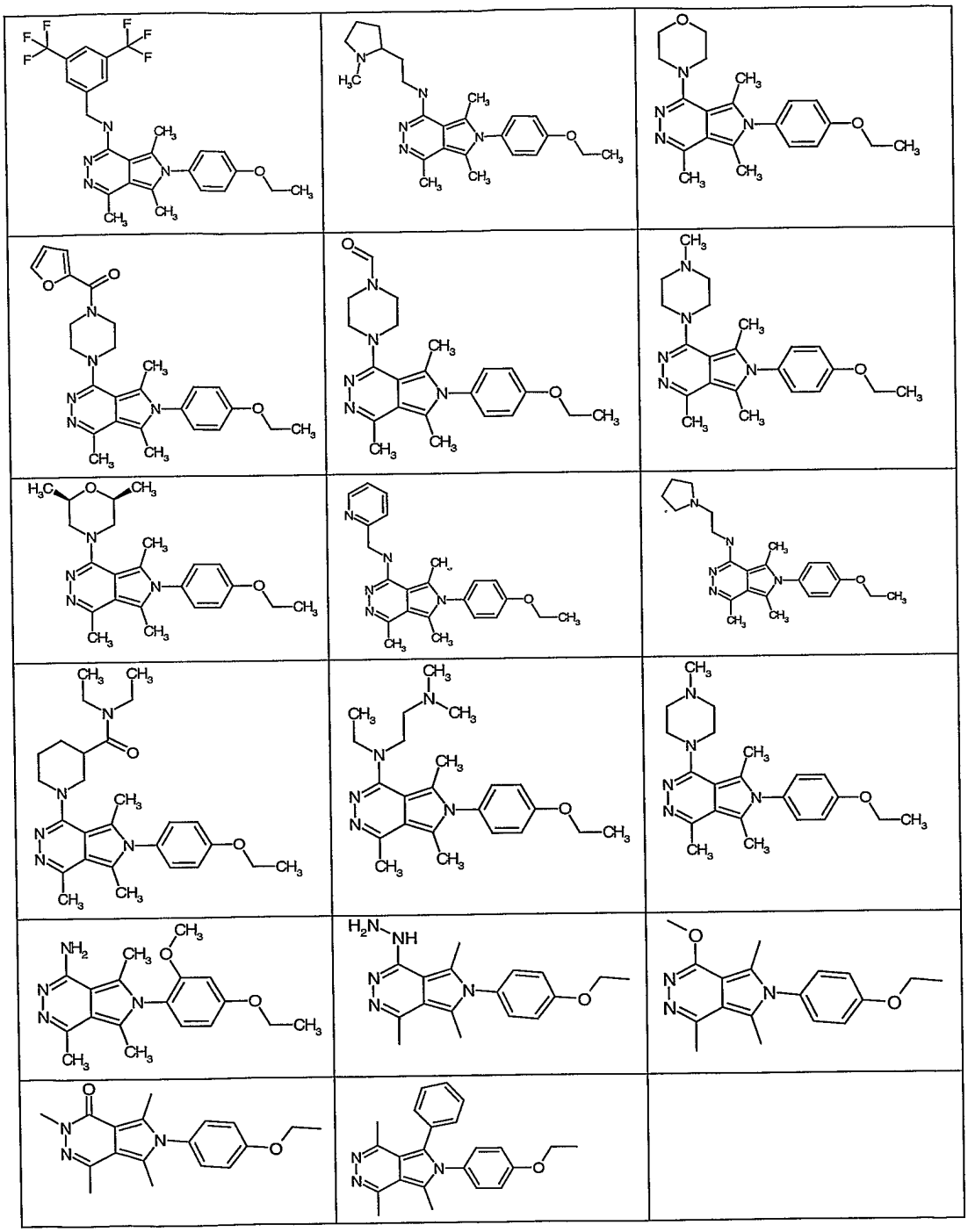







Chiral





or a pharmaceutically acceptable salt thereof.

5. A method of treatment of neuropathic pain comprising a step of administering an effective amount of a pharmaceutical composition comprising:

a therapeutically effective amount of the compound according to claim 1, or a pharmaceutically acceptable salt thereof; and

a pharmaceutically acceptable carrier.

6. The method according to claim 5, wherein said composition further comprising i) an opiate agonist, ii) an opiate antagonist, iii) an mGluR5 antagonist, iv) a 5HT receptor agonist, v) a 5HT receptor antagonist, vi) a sodium channel antagonist, vii) an NMDA receptor agonist, viii) an NMDA receptor antagonist, ix) a COX-2 selective inhibitor, x) an NK1 antagonist, xi) a non-steroidal anti-inflammatory drug, xii) a GABA-A receptor modulator, xiii) a dopamine agonist, xiv) a dopamine antagonist, xv) a selective serotonin reuptake inhibitor, xvi) a tricyclic antidepressant drug, xvii) a norepinephrine modulator, xviii) L-DOPA, xix) buspirone, xx) a lithium salt, xxi) valproate, xxii) neurontin, xxiii) olanzapine, xxiv) a nicotinic agonist, xxv) a nicotinic antagonist, xxvi) a muscarinic agonist, xxvii) a muscarinic antagonist, xxviii) a selective serotonin and norepinephrine reuptake inhibitor (SSNRI), xxix) a heroin substituting drug, xxx) disulfiram, or xxxi) acamprosate.

7. The method according to claim 6, wherein said heroin substituting drug is methadone, levo-alpha-acetylmethadol, buprenorphine or naltrexone.

8. A method of treatment or prevention of pain comprising the step of administering a therapeutically effective amount, or a prophylactically effective amount, of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

9. A method of treatment or prevention of a pain disorder wherein said pain disorder is acute pain, persistent pain, chronic pain, inflammatory pain, or neuropathic pain, comprising the step of administering a therapeutically effective amount, or a prophylactically effective amount, of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

10. A method of treatment or prevention of anxiety, depression, bipolar disorder, psychosis, drug withdrawal, tobacco withdrawal, memory loss, cognitive impairment, dementia, Alzheimer's disease, schizophrenia or panic comprising the

step of administering a therapeutically effective amount, or a prophylactically effective amount, of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

11. A method of treatment or prevention of disorders of extrapyramidal motor function comprising the step of administering a therapeutically effective amount, or a prophylactically effective amount, of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

12. The method of claim 11 wherein said disorder of extrapyramidal motor function is Parkinson's disease, progressive supramuscular palsy, Huntington's disease, Gilles de la Tourette syndrome, or tardive dyskinesia.

13. A method of treatment or prevention of anxiety disorders comprising the step of administering a therapeutically effective amount, or a prophylactically effective amount, of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

14. The method of claim 13 wherein said anxiety disorder is panic attack, agoraphobia or specific phobias, obsessive-compulsive disorders, post-traumatic stress disorder, acute stress disorder, generalized anxiety disorder, eating disorder, substance-induced anxiety disorder, or nonspecified anxiety disorder.

15. A method of treatment or prevention of neuropathic pain comprising the step of administering a therapeutically effective amount, or a prophylactically effective amount, of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

16. A method of treatment or prevention of Parkinson's Disease comprising the step of administering a therapeutically effective amount, or a prophylactically effective amount, of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

17. A method of treatment or prevention of depression comprising the step of administering a therapeutically effective amount, or a prophylactically

effective amount, of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

18. A method of treatment or prevention of epilepsy comprising the step of administering a therapeutically effective amount, or a prophylactically effective amount, of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

19. A method of treatment or prevention of inflammatory pain comprising the step of administering a therapeutically effective amount, or a prophylactically effective amount, of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

20. A method of treatment or prevention of cognitive dysfunction comprising the step of administering a therapeutically effective amount, or a prophylactically effective amount, of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

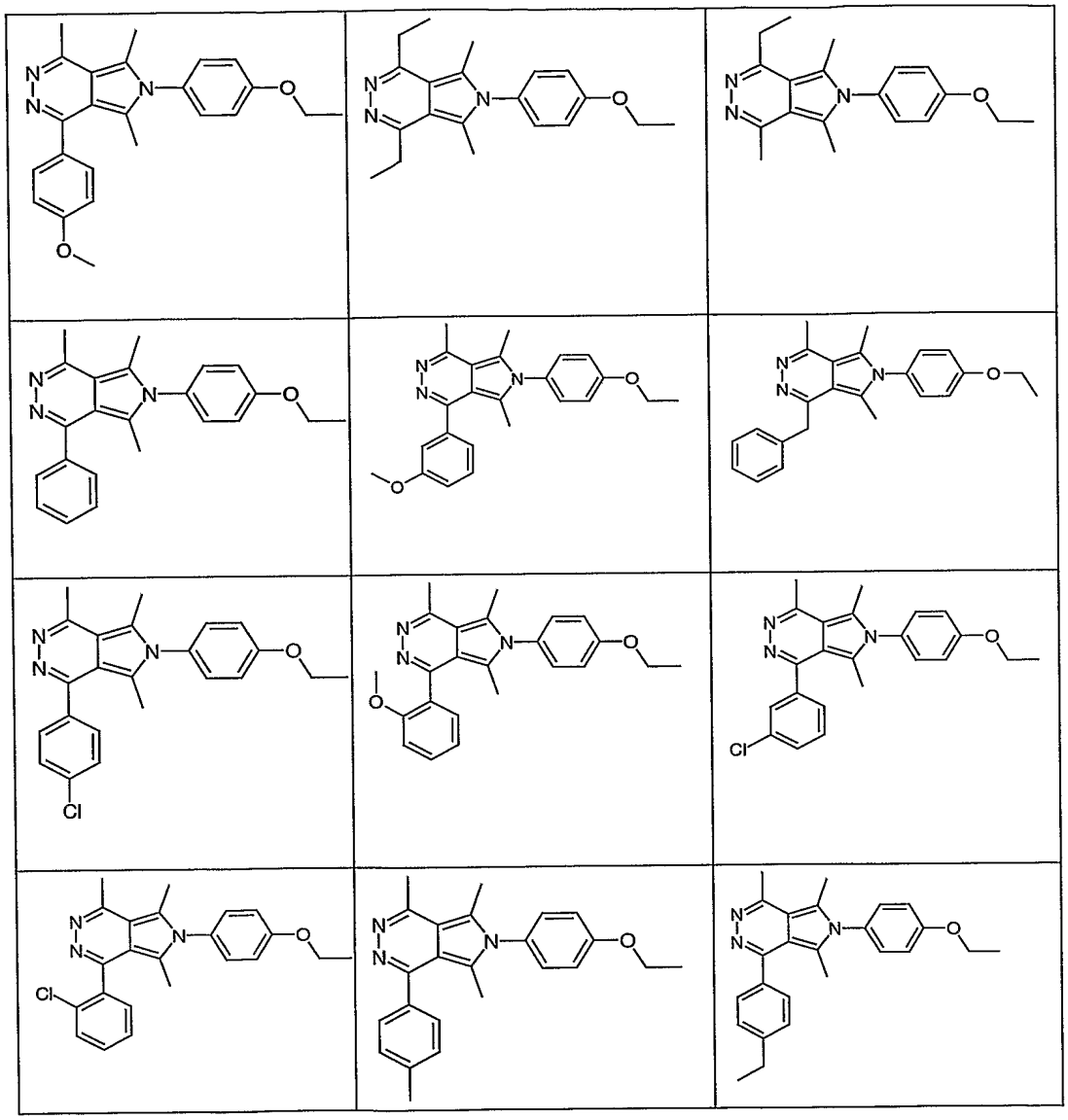
21. A method of treatment or prevention of drug addiction, drug abuse and drug withdrawal comprising the step of administering a therapeutically effective amount, or a prophylactically effective amount, of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

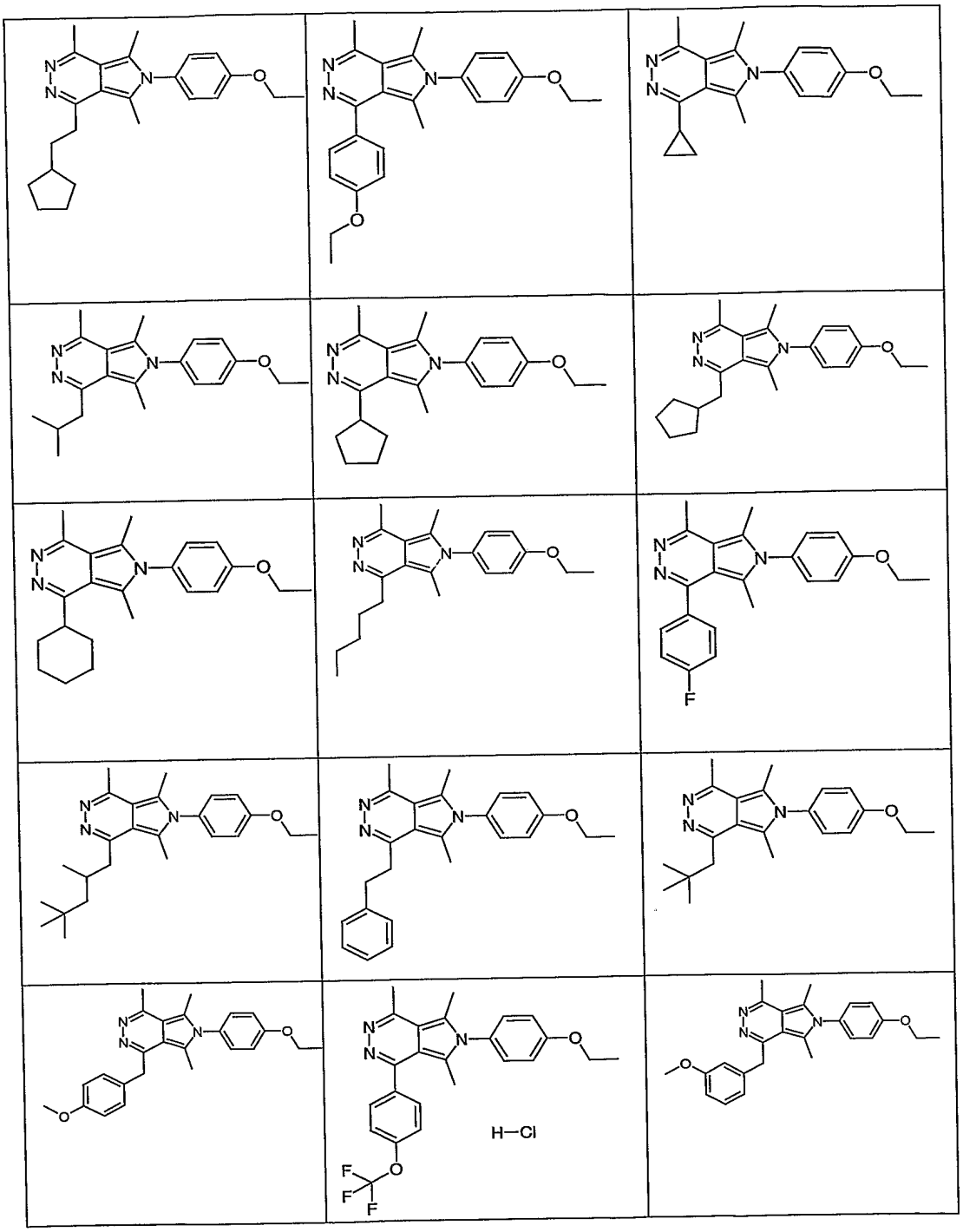
22. A method of treatment or prevention of bipolar disorders comprising the step of administering a therapeutically effective amount, or a prophylactically effective amount, of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

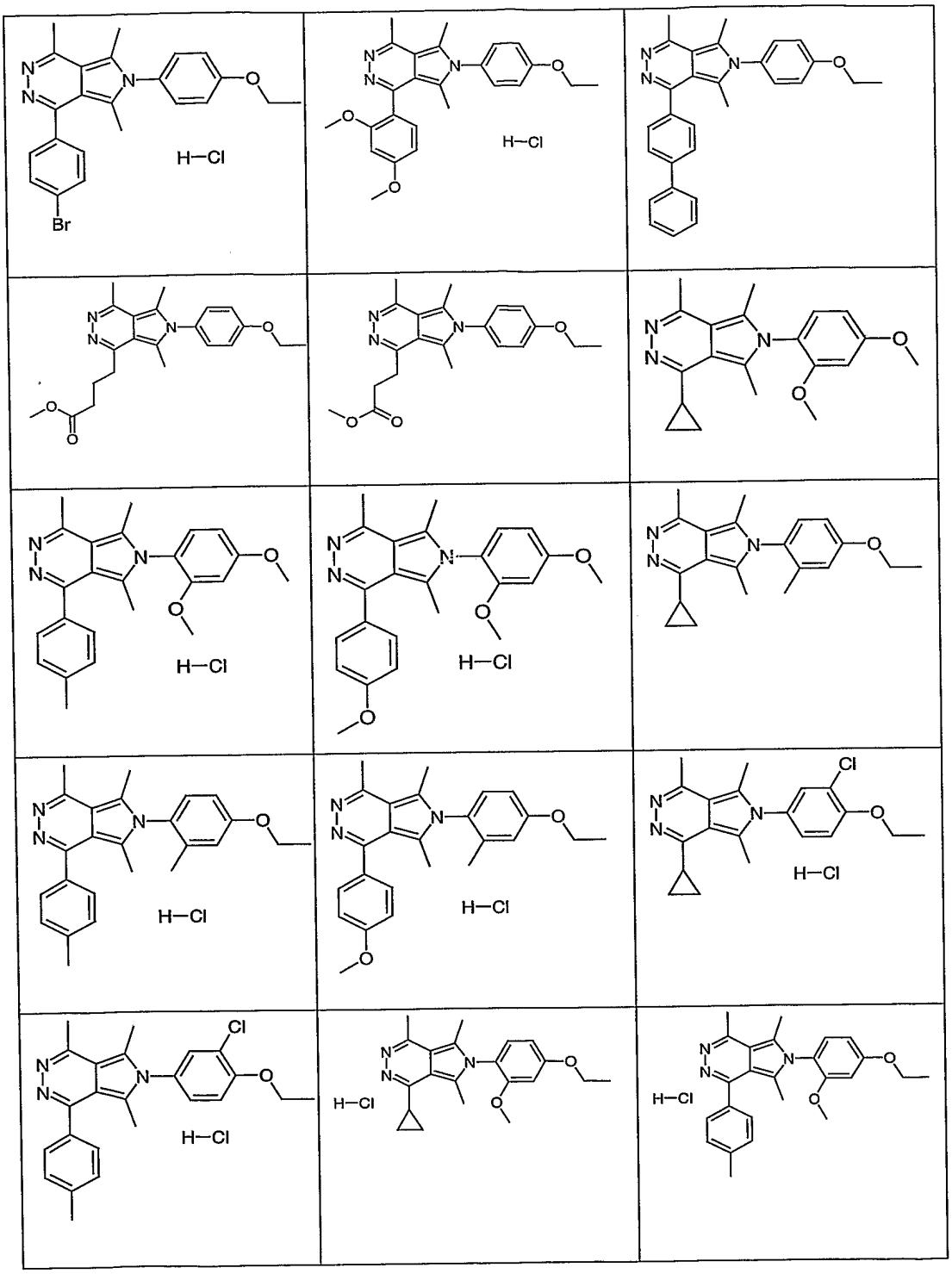
23. A method of treatment or prevention of circadian rhythm and sleep disorders comprising the step of administering a therapeutically effective amount, or a prophylactically effective amount, of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

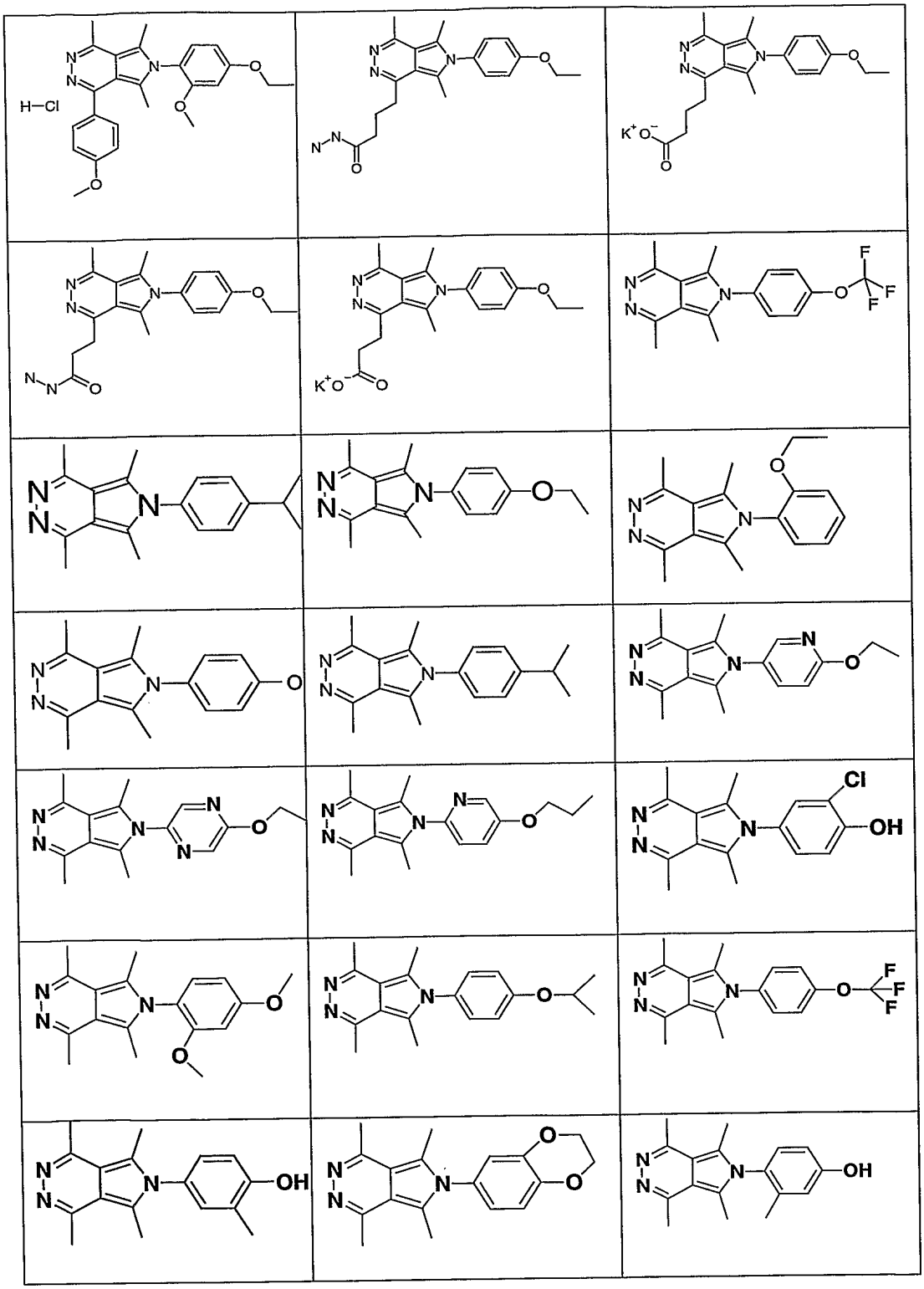
24. The method of Claim 23 wherein the circadian rhythm and sleep disorders are shift-work induced sleep disorder or jet-lag.

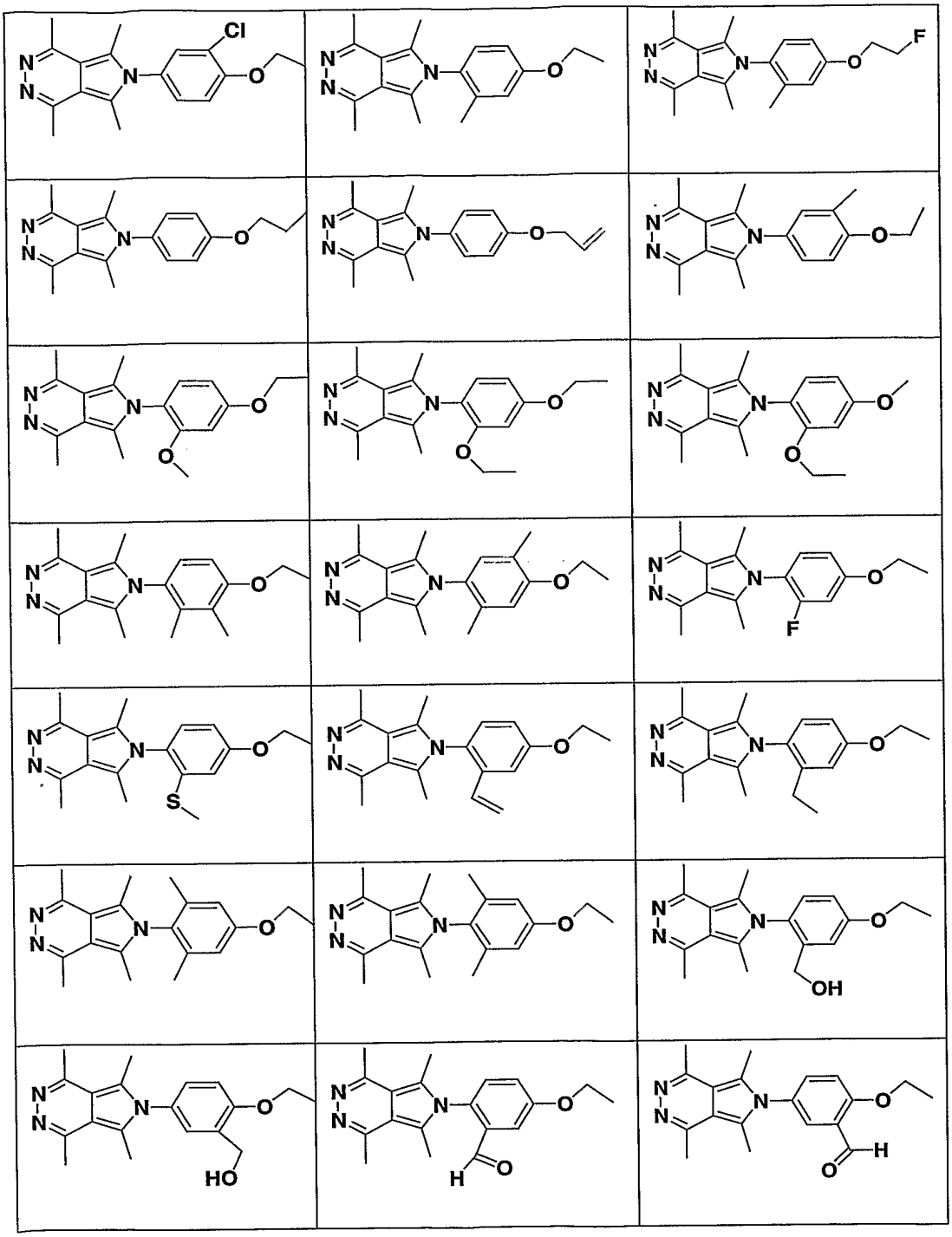
25. A compound selected from:

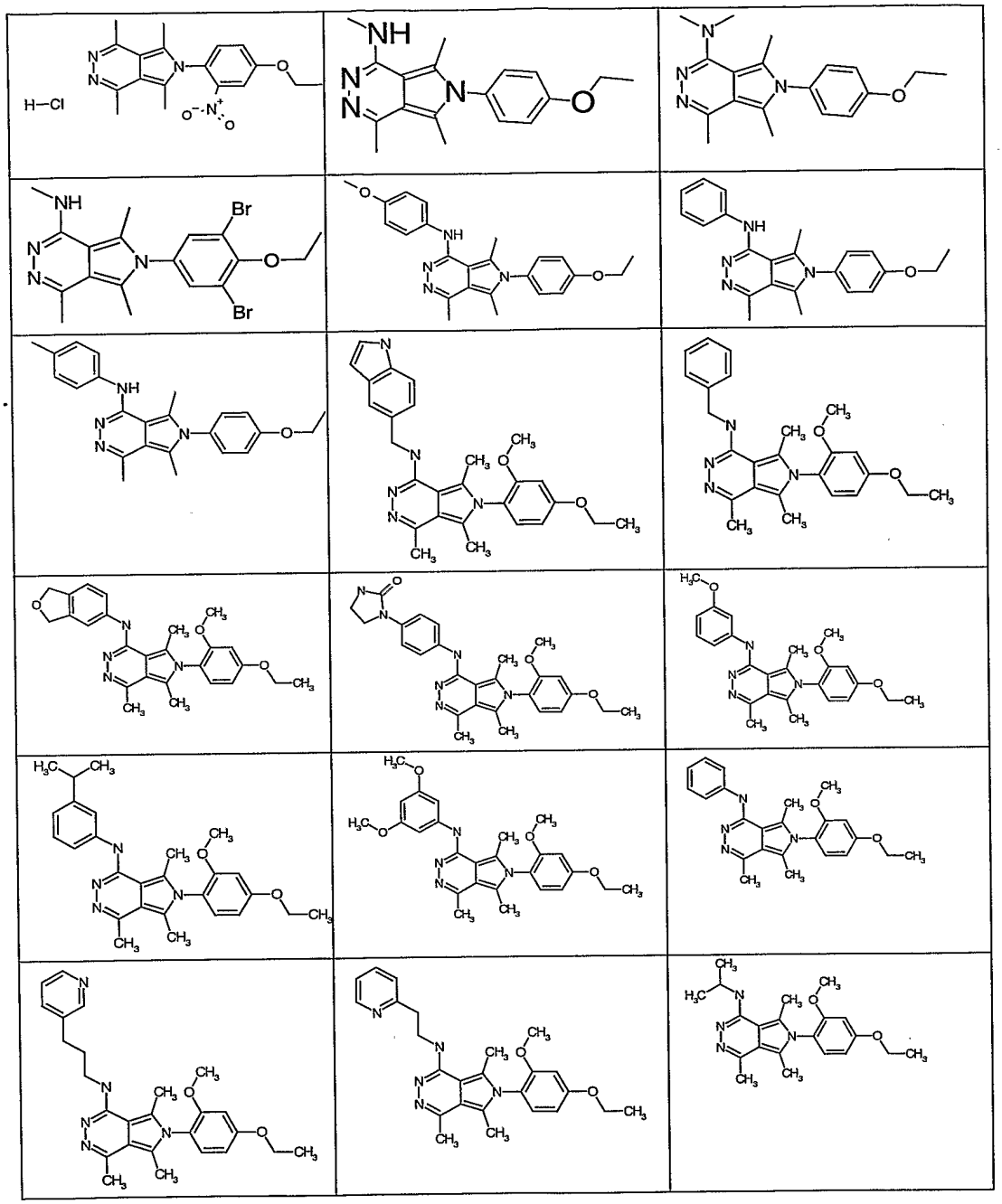


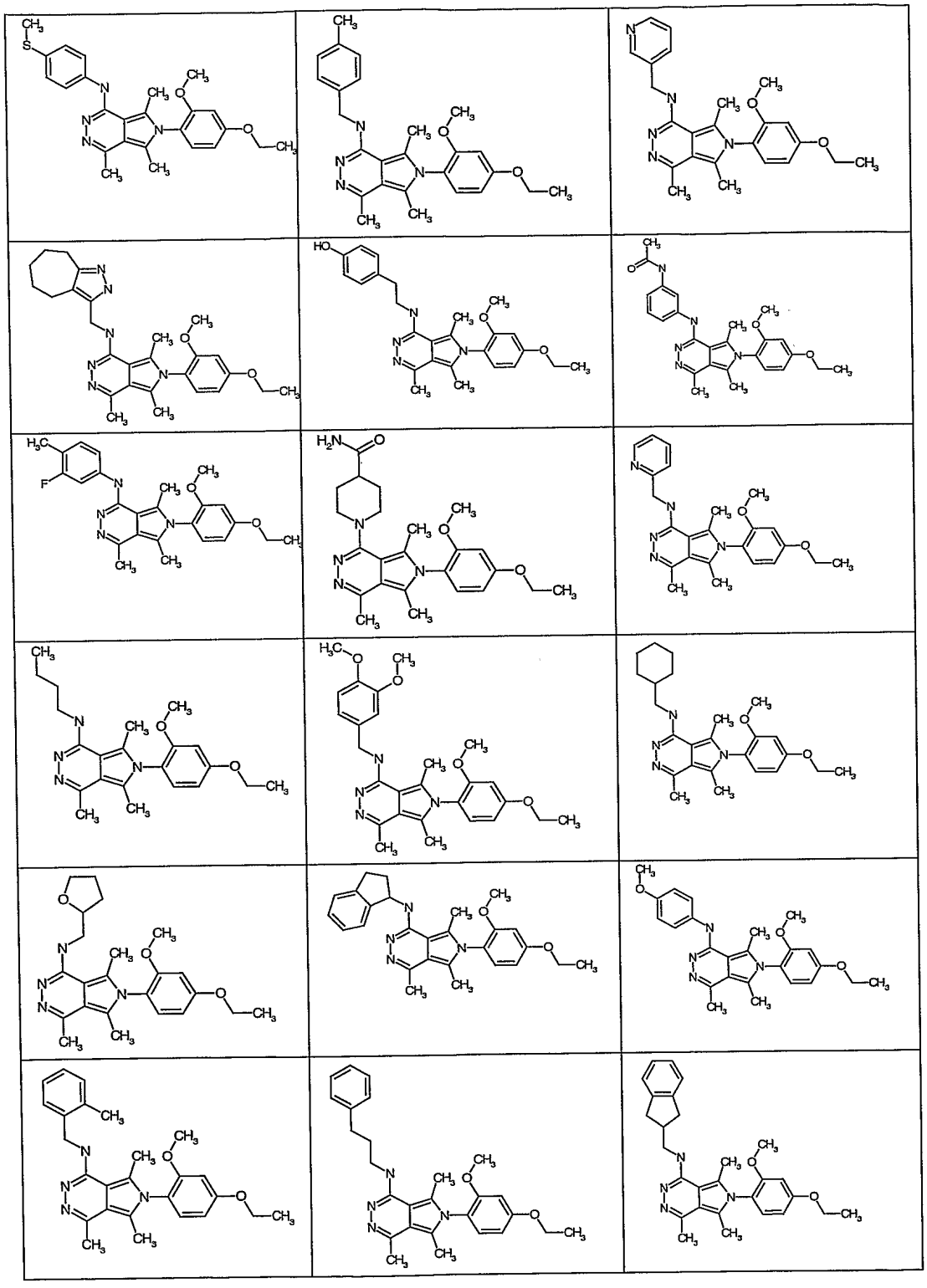

F
H—Cl
F
F
F

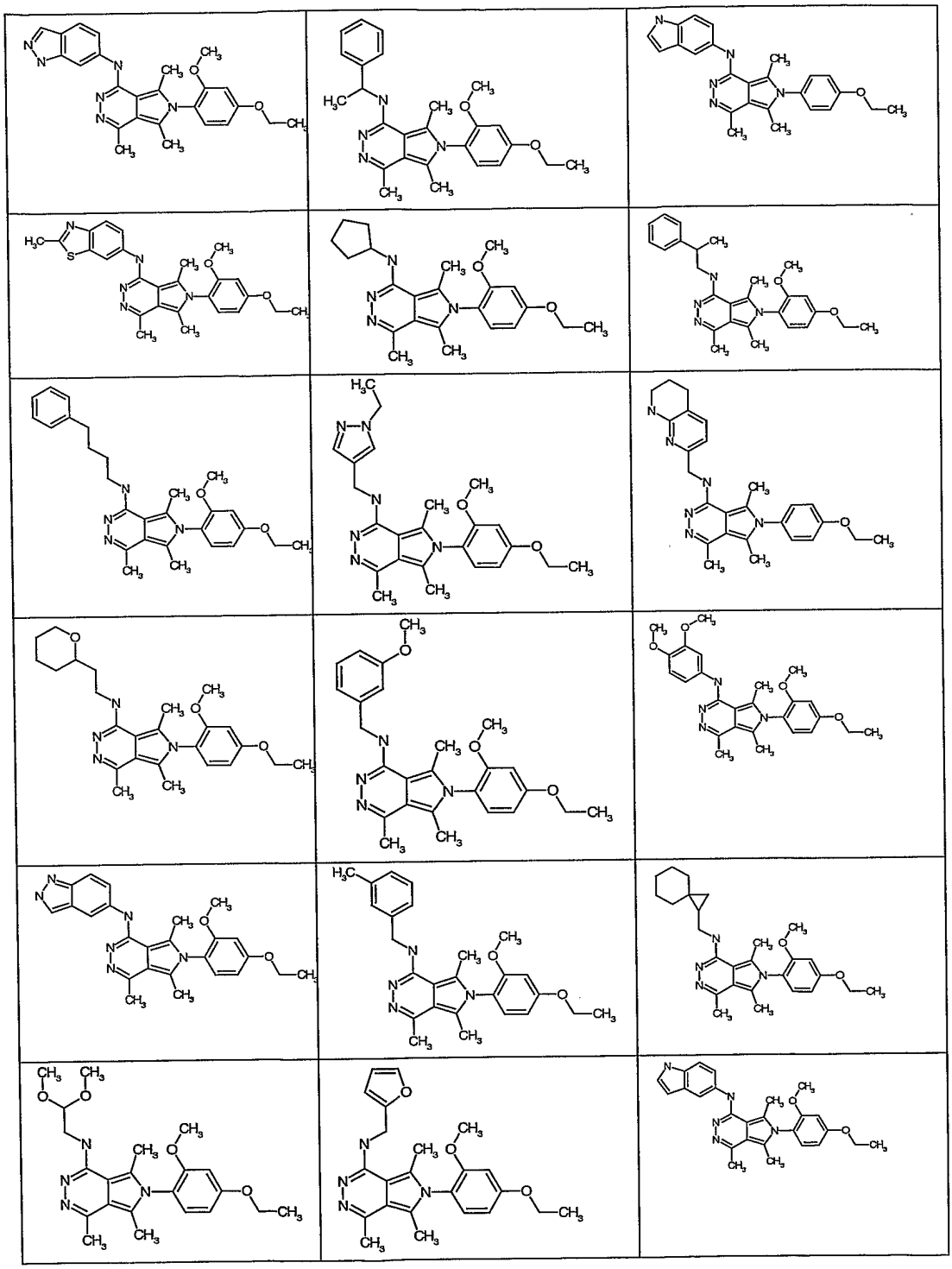

H–Cl
Br
H–Cl
H–Cl
H–Cl
H–Cl
H–Cl
Cl
H–Cl
Cl
H–Cl
H–Cl

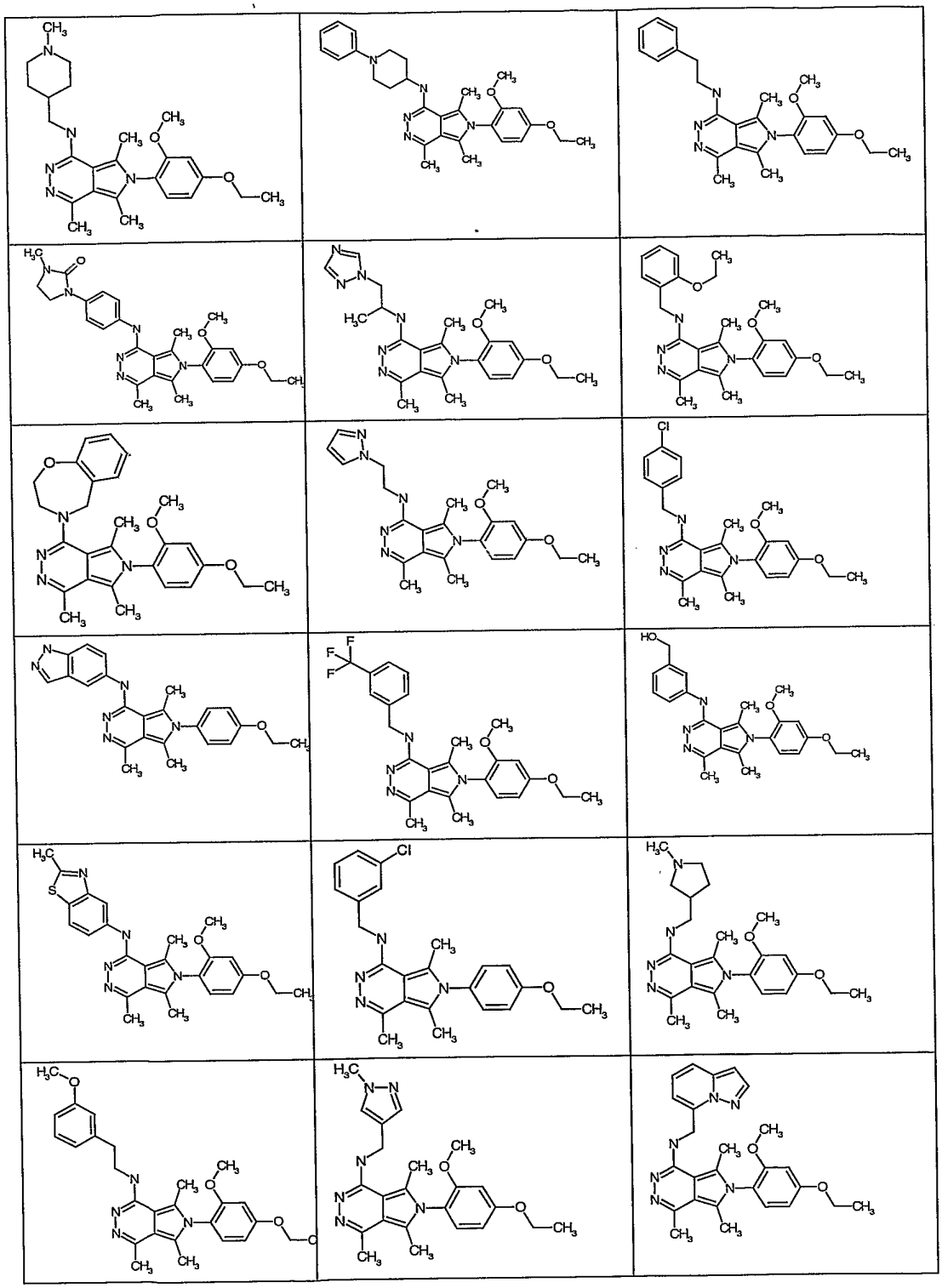


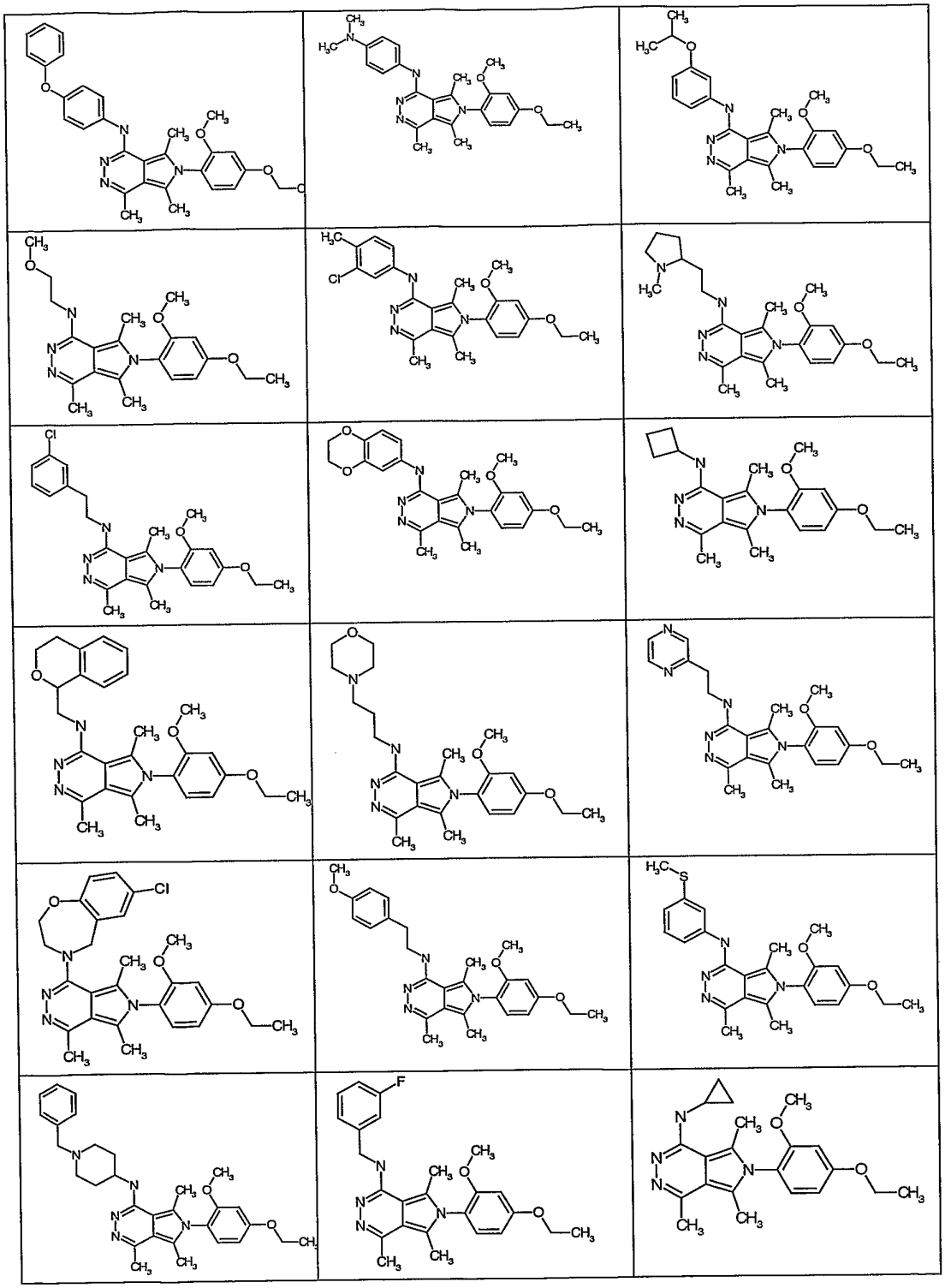


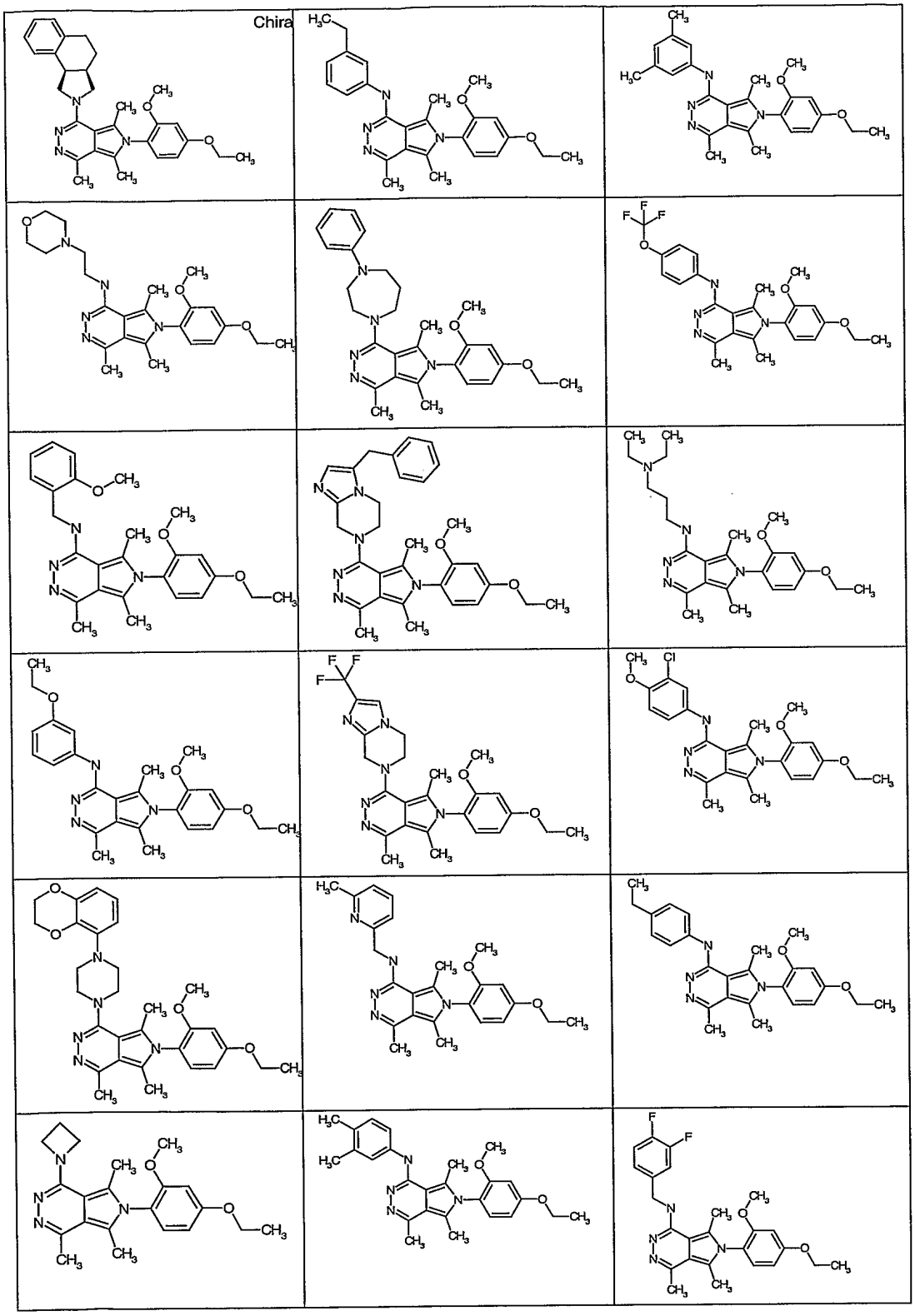








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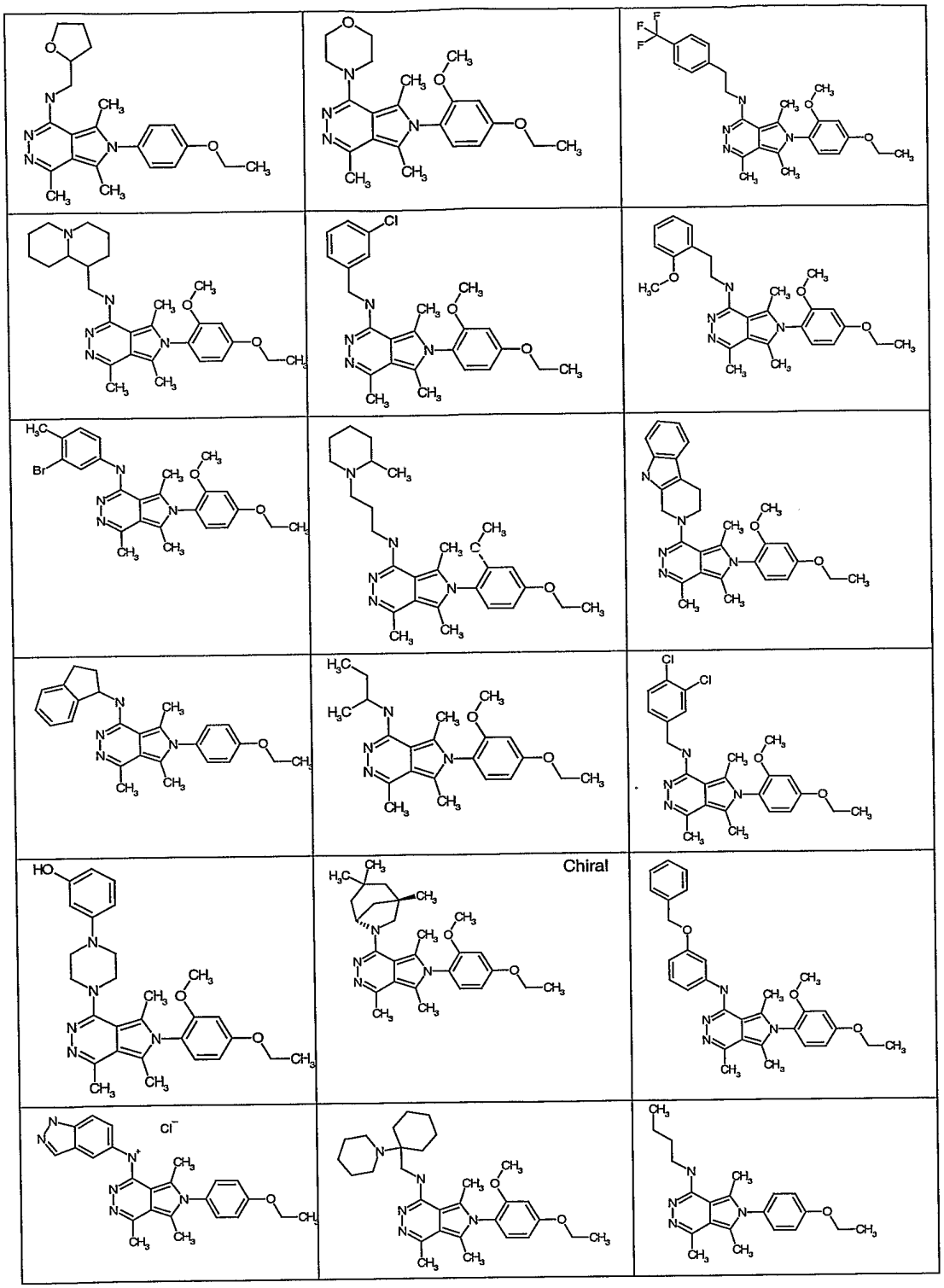
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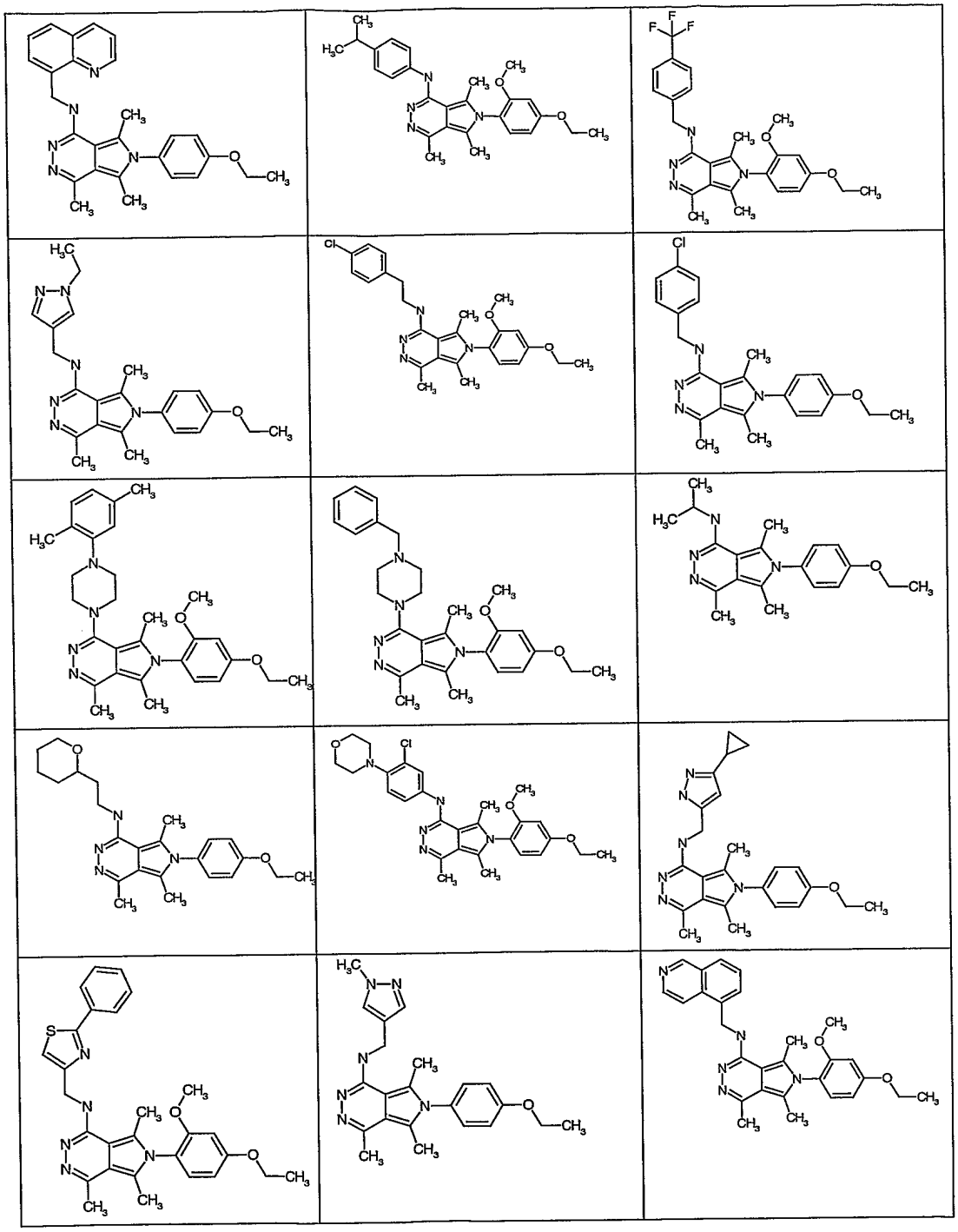
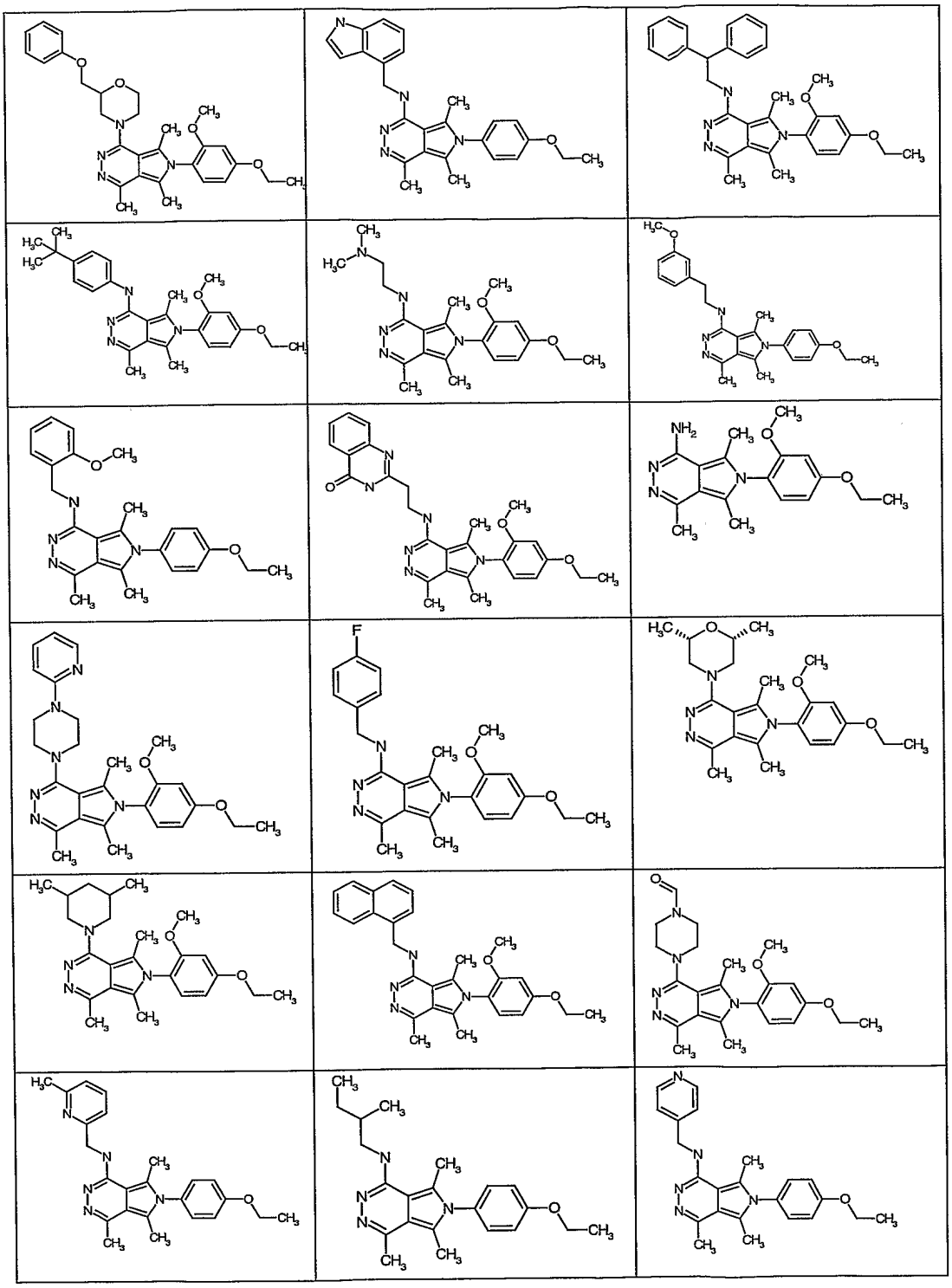
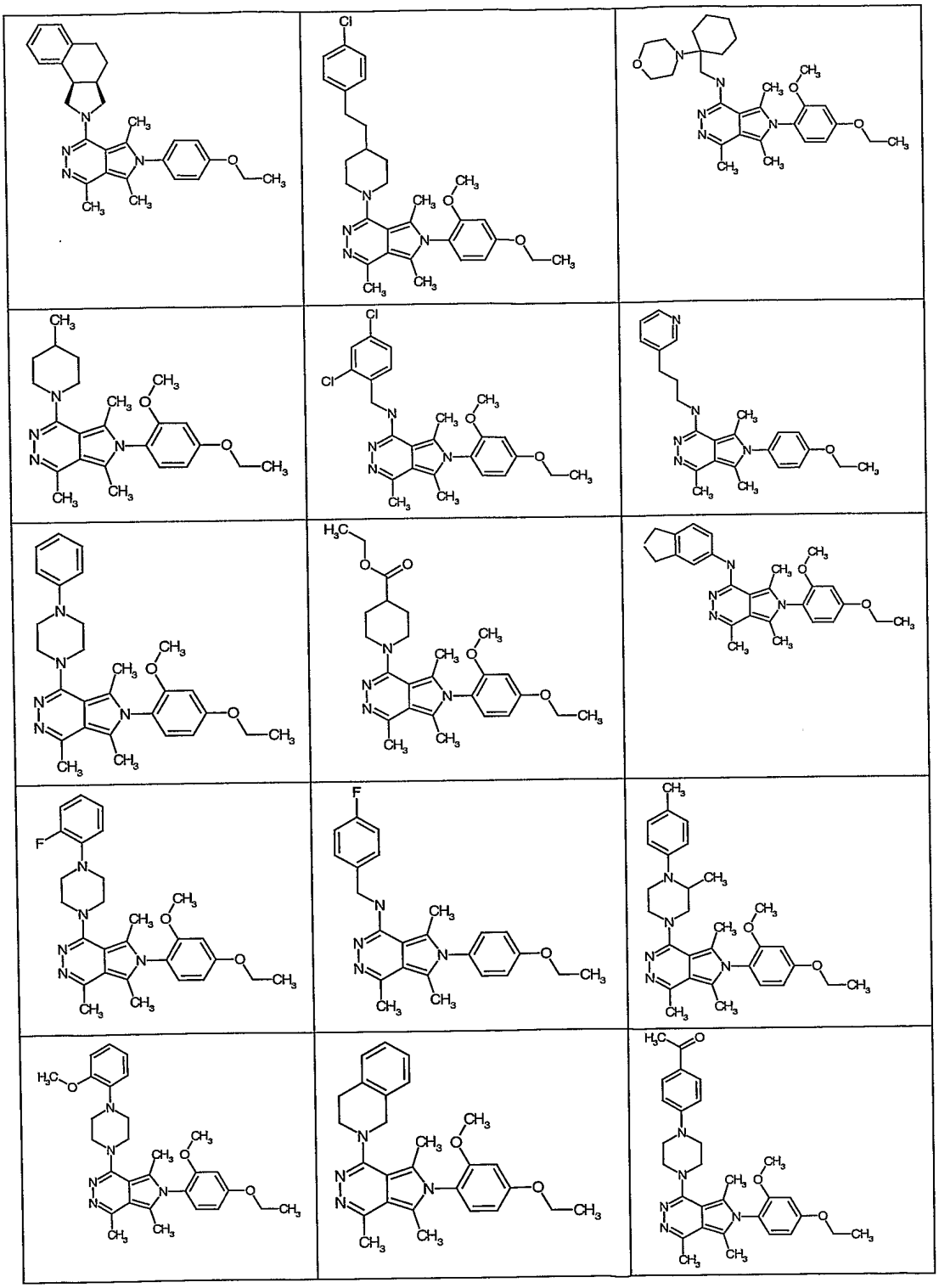
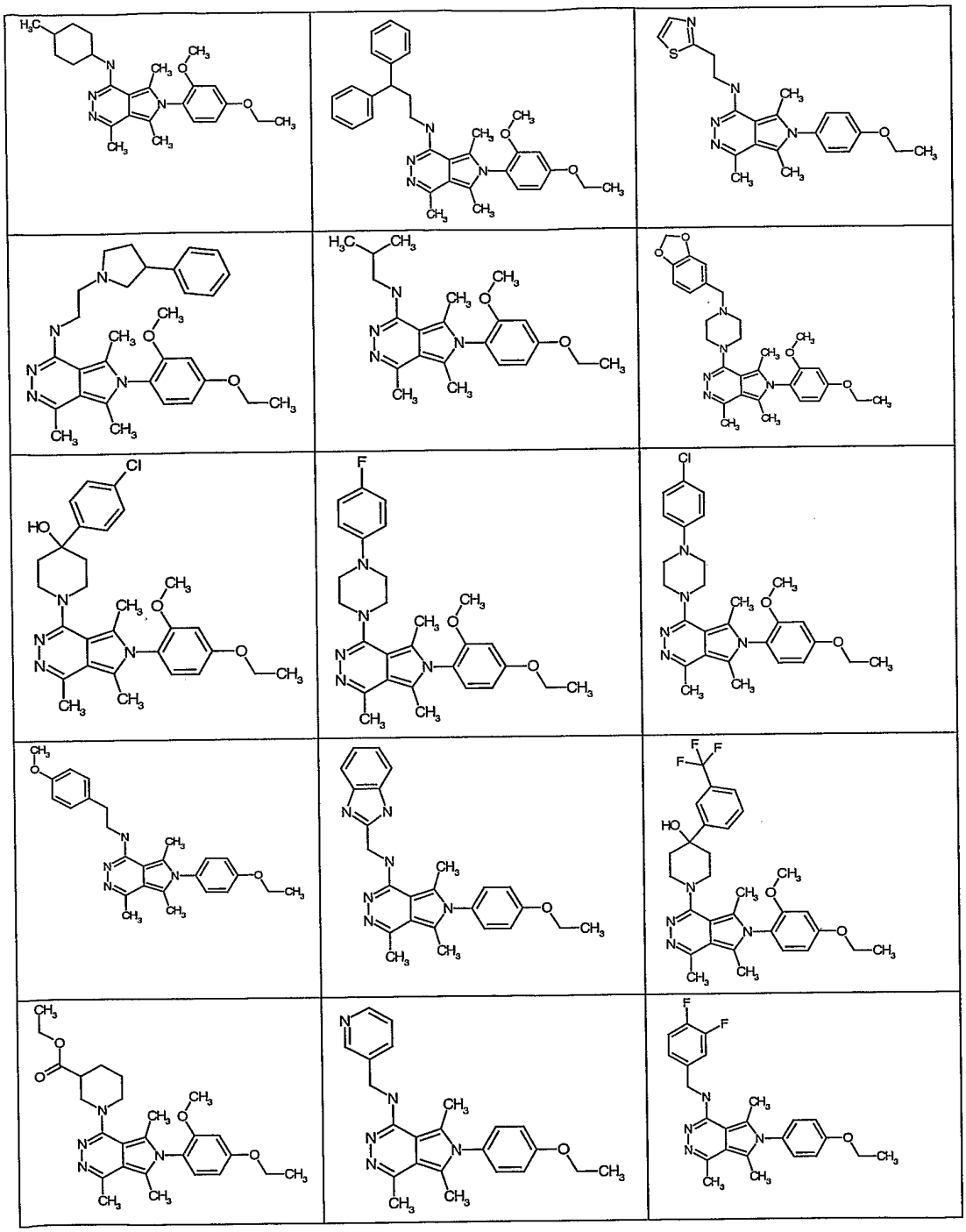
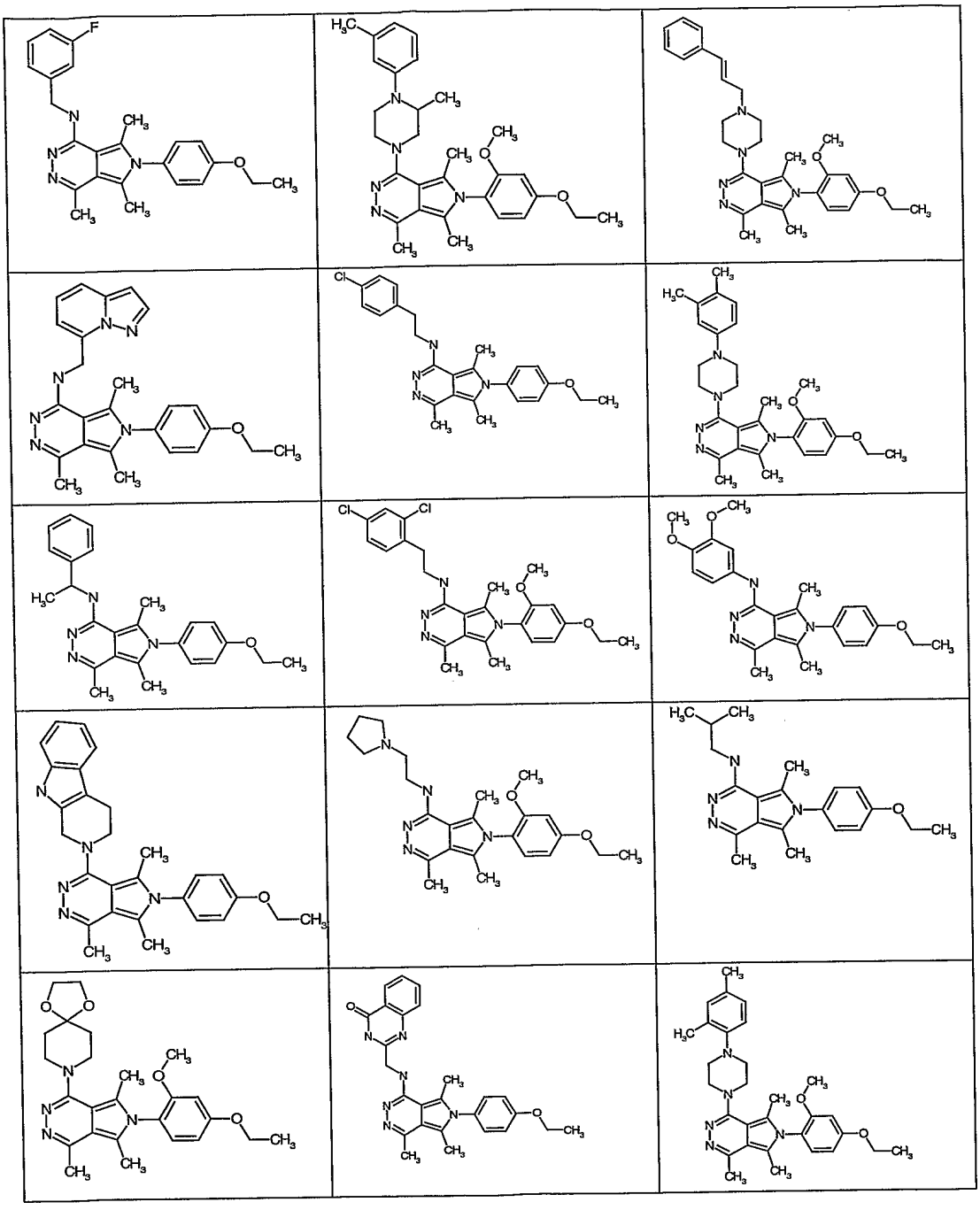
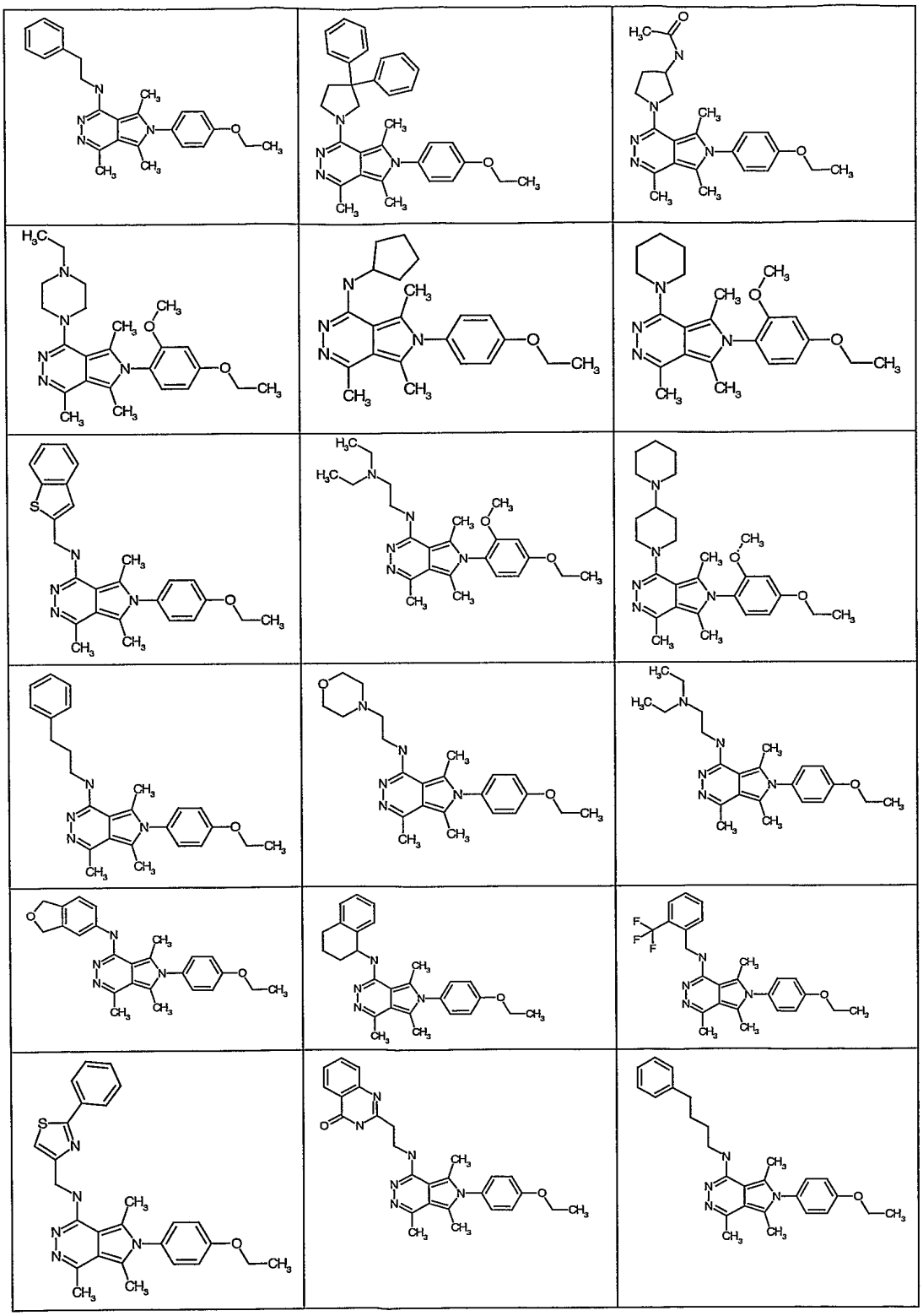


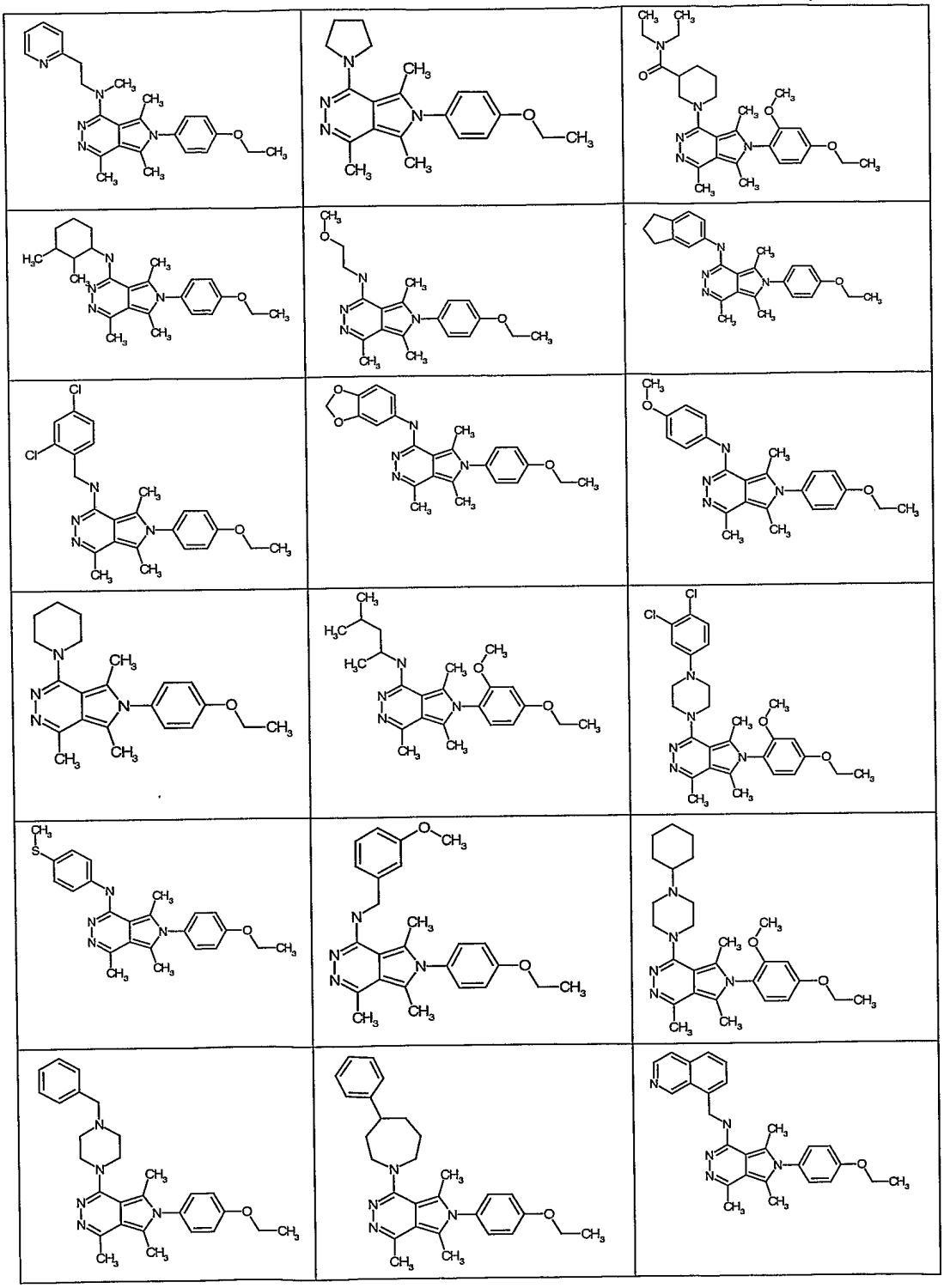


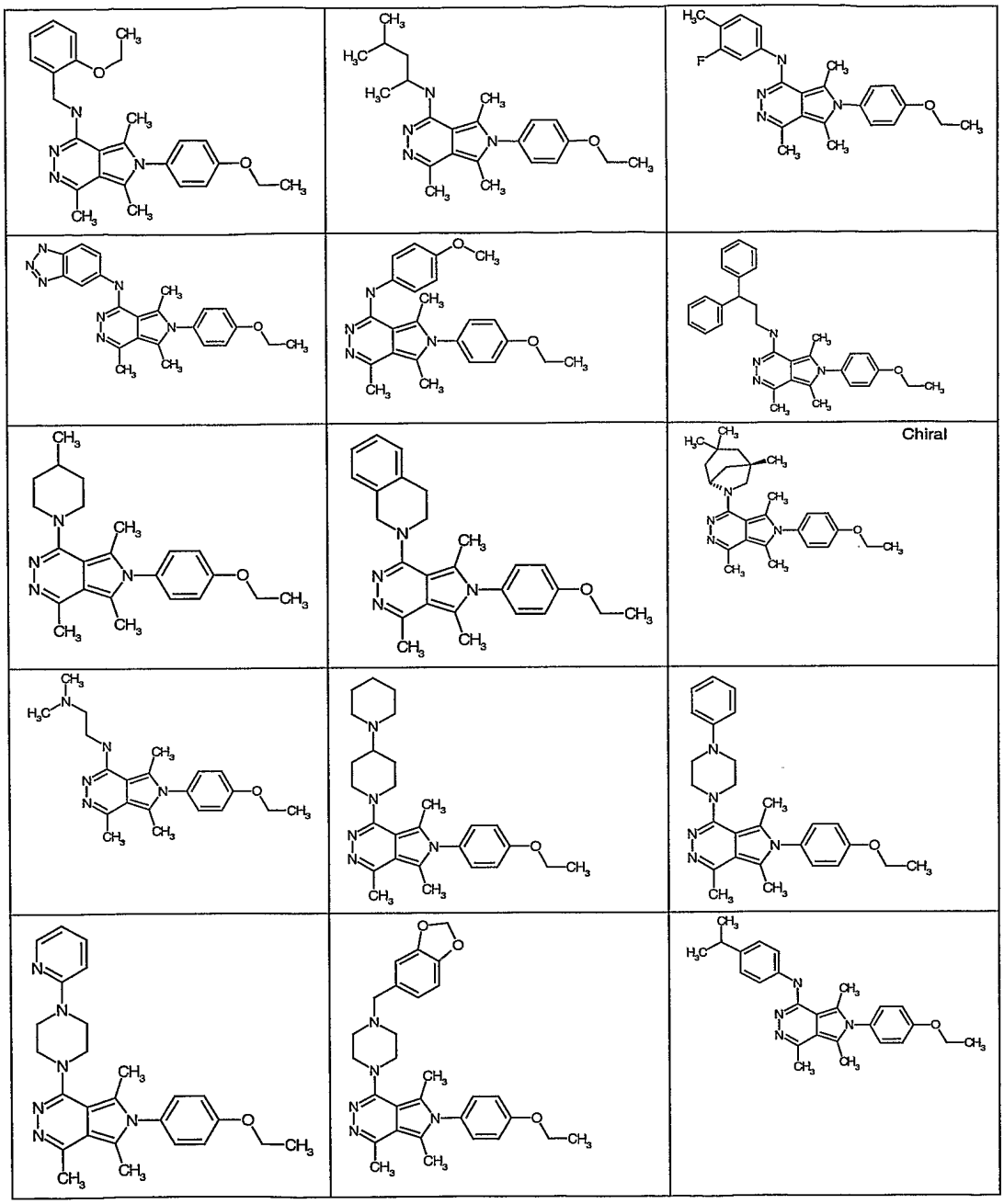


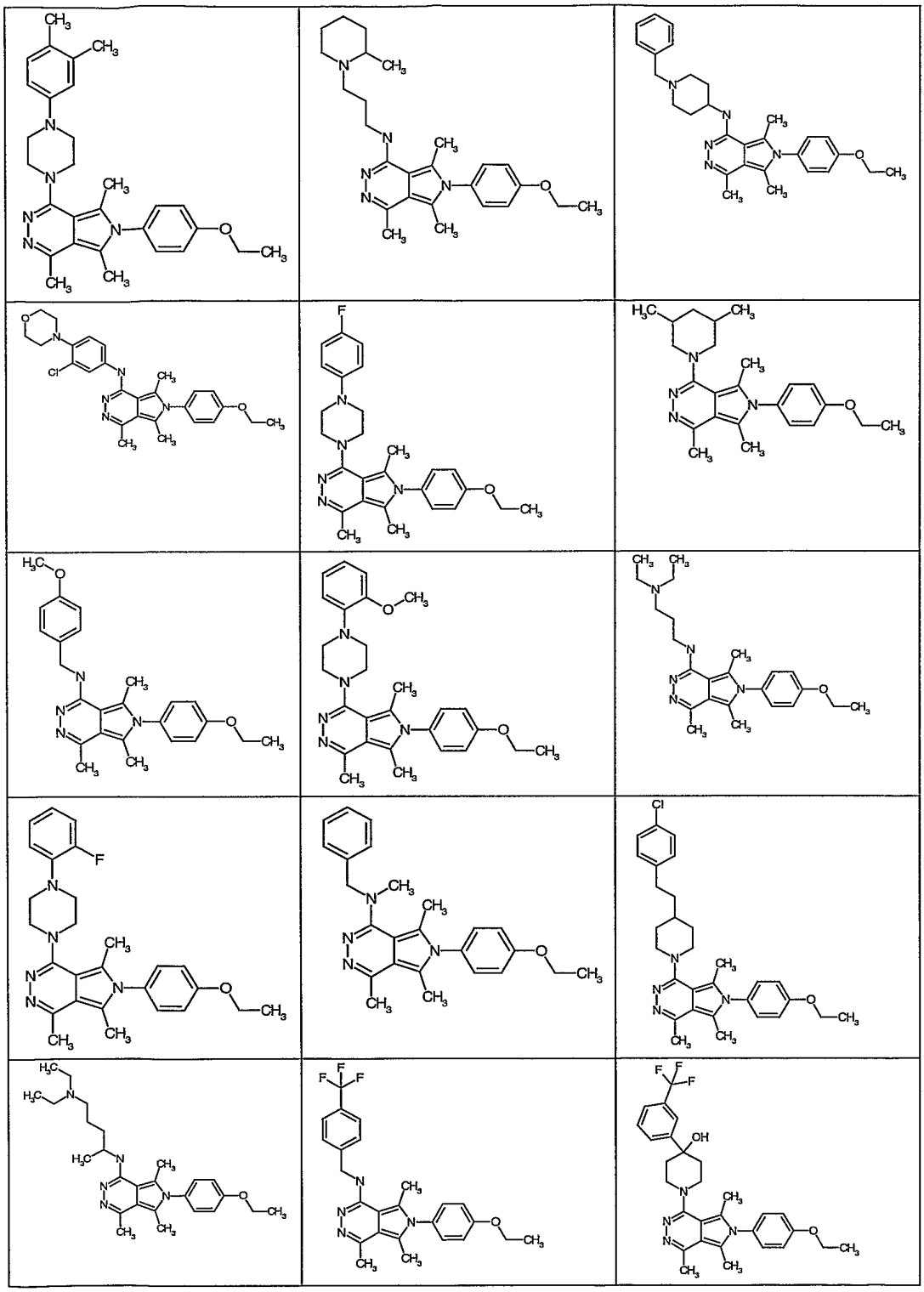


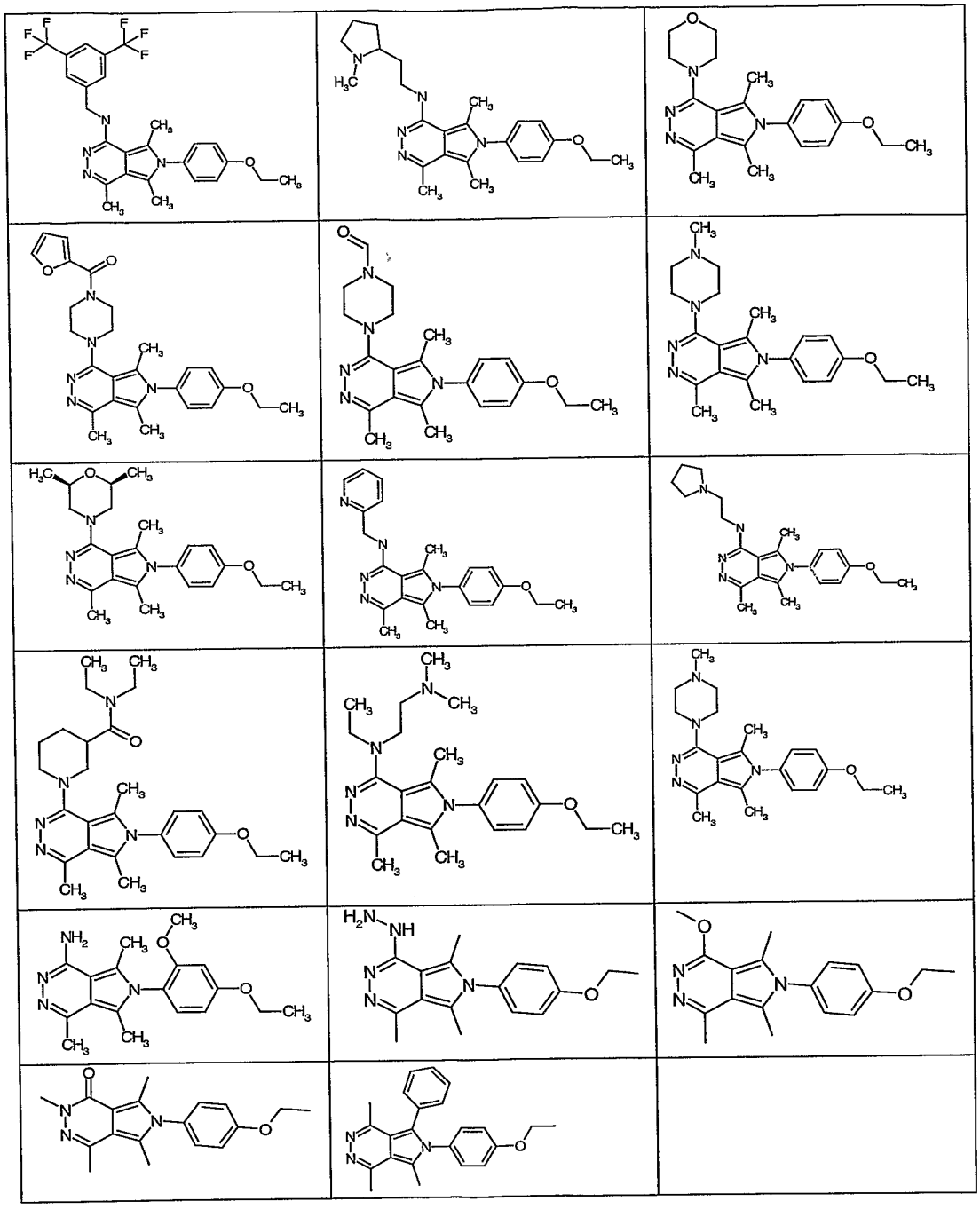







Chiral

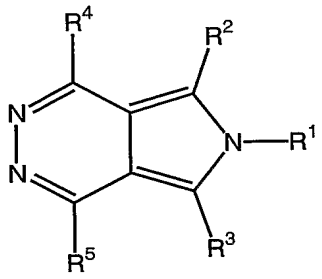




or a pharmaceutically acceptable salt thereof.

5

26. A compound represented by Formula (I):



(I)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is $-C_{0-6}$alkyl–aryl, $-C_{0-6}$alkyl–heteroaryl, $-C_{0-6}$alkyl–C_{3-6}cycloalkyl, or $-C_{0-6}$alkyl–heteroC_{3-7}cycloalkyl, optionally substituted with 1-6 independent halogen, –CN, NO_2, -C_{1-6}alkyl, $-C_{0-6}$alkyl–C_{3-6}cycloalkyl, $-C_{0-6}$alkyl–heteroC_{3-7}cycloalkyl, $-OR^6$, $-NR^6R^7$, $-C(=NR^6)NR^7R^8$, $-N(-NR^{88}R^6)NR^7R^8$, $-NR^6COR^7$, $-NR^6CO_2R^7$, $-NR^6SO_2R^{88}$, $-NR^6CONR^7R^8$, $-SR^{88}$, $-SOR^{88}$, $-SO_2R^{88}$, $-SO_2NR^6R^7$, $-COR^6$, $-CO_2R^6$, $-CONR^6R^7$, $-C(=NR^6)R^7$, or $-C(=NOR^6)R^7$ substituents;

R^2, R^4, R^3, and R^5 each independently is $-C_{0-6}$alkyl, $-C_{0-6}$alkyl–aryl, $-C_{0-6}$alkyl–heteroaryl, $-C_{0-6}$alkyl–C_{3-6}cycloalkyl, or $-C_{0-6}$alkyl–heteroC_{3-7}cycloalkyl, optionally substituted with 1-6 independent halogen, –CN, NO_2, -C_{1-6}alkyl, $-OR^6$, $-NR^6R^7$, $-C(=NR^6)NR^7R^8$, $-N(-NR^{88}R^6)NR^7R^8$, $-NR^6COR^7$, $-NR^6CO_2R^7$, $-NR^6SO_2R^{88}$, $-NR^6CONR^7R^8$, $-SR^{88}$, $-SOR^{88}$, $-SO_2R^{88}$, $-SO_2NR^6R^7$, $-COR^6$, $-CO_2R^6$, $-CONR^6R^7$, $-C(=NR^6)R^7$, or $-C(=NOR^6)R^7$ substituents; and

R^6, R^7, R^8, and R^{88} each independently is $-C_{0-6}$alkyl, $-C_{3-7}$cycloalkyl, heteroaryl, or aryl; optionally substituted with 1-5 independent halogen, -CN, $-C_{1-6}$alkyl, $-O(C_{0-6}$alkyl), $-O(C_{3-7}$cycloalkyl), -O(aryl), $-N(C_{0-6}$alkyl)(C_{0-6}alkyl), $-N(C_{0-6}$alkyl)(C_{3-7}cycloalkyl), or $-N(C_{0-6}$alkyl)(aryl) substituents; provided that the compound is not

6-methyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

1,4,5,7-tetramethyl-6-phenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

1,4,5-trimethyl-6,7-diphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

5,7-dimethyl-1,4,6-triphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

5-methyl-1,4,6,7-tetraphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

1,4-bis-(4-methoxy-phenyl)-5,7-dimethyl-6-phenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

1,4-bis-(4-methoxy-phenyl)-5-methyl-6,7-diphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

1,4-diethyl-5,7-dimethyl-6-phenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

1,4,5,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

N-(1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-yl)-benzamide,

1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-ylamine picrate,

1,4,5,7-tetramethyl-pyrrolo[3,4-*d*]pyridazin-6-ylamine,

5,7-dimethyl-6-phenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

5,7-dimethyl-2-phenacyl-6*H*-pyrrolo[3,4-*d*]pyridazinium bromide,

2-(2-methoxycarbonylvinyl)-5,7-dimethyl-6*H*-pyrrolo[3,4-*d*]pyridazinium tetrafloroborate

5,7-diphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

5,6,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

1,4-diphenyl-7,8,9,10-tetrahydro-pyridazino[4,5-*a*]indolizine,

5-methyl-1,4-diphenyl-7,8,9,10-tetrahydro-pyridazino[4,5-*a*]indolizine,

6-benzyl-1,4-diphenyl-5-p-tolyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

6-benzyl-5-(2-chloro-phenyl)-1,4-diphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

1,4,5,6,7-pentaphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

6,7,10,11-tetraphenyl-pyridazino[4',5':3,4]pyrrolo[1,2-*a*]quinoxaline,

11-(4-nitro-phenyl)-6,7,10-triphenyl-pyridazino[4'.5':3,4]pyrrolo[1,2-*a*]quinoxaline,

6-benzyl-1,4,5-triphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

9,12-diphenyl-pyridazino[4',5':3,4]pyrrolo[2,1-*a*]isoquinoline,

5-methylsulfanyl-1,4,6,7-tetraphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine,

1,4,6,7-tetraphenyl-6*H*-pyrrolo[3,4-*d*]pyridazine-5-carboxylic acid ethyl ester,

7,10-diphenyl-pyridazino[4',5':3,4]pyrrolo[1,2-*a*]quinoline,

11,14-diphenyl-pyridazino[4',5':3,4]pyrrolo[1,2-*f*]phenanthridine,

1-oxo-7-oxy-6b,11b-dihydro(pyridazino[4',5'-c]-pyrrolo)[2.1-c]benzoxazine-1,4,

10-methyl-1,4-diphenyl-8,9-dihydro-7H-benzo(ef)pyridazino[4,5-a]cycl[3.3.2]azine,

11-methyl-1,4-diphenyl-7,8,9,10-tetrahydrocyclohepta(ef)pyridazino[4,5-a]cycl[3.3.2]azine,
1,4-dichloro-5,6,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine,
1-chloro-4-ethoxy-5,6,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine,
1-chloro-5,6,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazinium chloride,
1-ethoxy-2,5,6,7-tetramethyl-6*H*-pyrrolo[3,4-*d*]pyridazinium tetrafluoroborate,
1-ethoxy-5,6,7-trimethyl-2*H*,6*H*-pyrrolo[3,4-*d*]pyridazinium tetrafluoroborate,
1-ethoxy-3-ethyl-5,6,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazinium tetrafluoroborate,
1-ethoxy-5,6,7-trimethyl-6*H*-pyrrolo[3,4-*d*]pyridazine,
5-cyano-1,4-dimethylpyridazino[4,5-*a*]indolizine,
1,4-dimethyl-6-phenyl-2,3,8a-triaza-fluorene-9-carbonitrile,
6-benzolyl-1,4-dimethyl-2,3,8a-triaza-fluorene-9-carbonitrile,
6-benzyl-1,4-diphenyl-2,3,8a-triaza-fluorene-9-carbonitrile,
1,4,6-trimethyl-2,3,8a-triaza-fluorene-9-carbonitrile,
5-cyano-1,4-diphenylpyridazino[4,5-*a*]indolizine,
6-methyl-1,4-diphenyl-2,3,8a-triaza-fluorene-9-carbonitrile,
6-benzoyl-1,4-diphenyl-2,3,8a-triaza-fluorene-9-carbonitrile,
1,4,6-triphenyl-2,3,8a-triaza-fluorene-9-carbonitrile,
5,7-dimethyl-1,4-diphenyl-2,3,8a-triaza-fluorene-9-carbonitrile,
9,12-diphenyl-pyridazino[4',5':3,4]pyrrolo[2,1-*a*]isoquinoline-8-carbonitrile,
dimethyl 3,12,13,17-tetramethyl-7^2,7^3-diazabenzo[g]porphyrin-2,18-dipropionate,
5,6-dihydro-2,3-dimethoxypyridazino[4',5':3,4]pyrrolo[2,1-*a*]isochinolin-9-ol,
5,6-dihydro-2,3-dimethoxypyridazino[4',5':3,4]pyrrolo[2,1-*a*]isochinolin-9-ol-hydrochloride,
3-methyl-6,9-diphenylthiazolo[3',2':1,2]pyrrolo[3,4-*d*]pyridine, or
1,4-diphenylpyridazino[4',5':3,4]pyrrolo[2,1-*b*]benzothiazole; and

is not selected from the following table: